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Columbia University, College of
Physicians & Surgeons. Dept. of
Physiology

STUDIES

FROM THE

DEPARTMENT OF PHYSIOLOGY

OF

COLUMBIA UNIVERSITY

AT THE

COLLEGE OF PHYSICIANS AND SURGEONS

NEW YORK

REPRINTS

1887–1897

Vol. I

102025
27/5/10

ISSUED BY

THE DEPARTMENT

CONTENTS.

Is the "Knee-Kick" a reflex act? By Warren P. Lombard. Reprinted from The American Journal of the Medical Sciences, 49, 1887.

On the nature of the knee jerk. By Warren P. Lombard. Reprinted from the Journal of Physiology, x, 1889.

On the respiratory changes of the intra-thoracic pressure measured in the mediastinum posterior. By S. J. Meltzer. Reprinted from the Journal of Physiology, xiii, 1892.

Ueber den Gleichgewichtssinn. By Frederic S. Lee. Reprinted from the Centralblatt für Physiologie, vi, 1892.

A study of the sense of equilibrium in fishes, I. By Frederic S. Lee. Reprinted from the Journal of Physiology, xv, 1893.

Notes upon some kymographic tracings of tremor. By Frederick Peterson. Reprinted from The New York Medical Journal, 59, 1894.

The scope of modern physiology. By Frederic S. Lee. Reprinted from The American Naturalist, xxviii, 1894.

Die zuckerbildende Function des N. Vagus. By P. A. Levene. Reprinted from the Centralblatt für Physiologie, viii, 1894.

A study of the sense of equilibrium in fishes, II. By Frederic S. Lee. Reprinted from the Journal of Physiology, xvii, 1894.

Studies in phloridzin glycosuria. By P. A. Levene. Reprinted from the Journal of Physiology, xvii, 1894.

An experimental study of direct and indirect faradization of the digestive canal in dogs, cats and rabbits. By S. J. Meltzer. Reprinted from The New York Medical Journal, 61, 1895.

On absorption of strychnine and hydrocyanic acid from the mucous membrane of the stomach. An experimental study on rabbits. By S. J. Meltzer. Reprinted from the Journal of Experimental Medicine, i, 1896.

The influence of phloridzin on the bile and lymph. By P. A. Levene. Reprinted from the Journal of Experimental Medicine, ii, 1897.

The bactericidal action of lymph taken from the thoracic duct of the dog. By S. J. Meltzer and Charles Norris. Reprinted from the Journal of Experimental Medicine, ii, 1897.

Notes on the physiology of the cardiac nerves of the opossum (Didelphys Virginiana). By R. Hunt and D. W. Harrington. Reprinted from The Journal of Experimental Medicine, ii, 1897.

Note on the physiology of the cardiac nerves of the calf. By R. Hunt and D. W. Harrington. Reprinted from the Journal of Experimental Medicine, ii, 1897.

Ueber Reizversuche mit Inductionsströmen am Tiermagen. By S. J. Meltzer. Reprinted from the Archiv für Verdauungskrankheiten, iii, 1897.

A further experimental contribution to the knowledge of the mechanism of deglutition. By S. J. Meltzer. Reprinted from the Journal of Experimental Medicine, ii, 1897.

The experiments on the faradization of the stomach of animals. A reply to Dr. M. Einhorn's criticism, with a communication of some new experiments. By S. J. Meltzer. Reprinted from the New York Medical Journal, 66, 1897.

Einige allgemeine Eigenschaften des Herzmuskels vom amerikanischen Hummer (Homarus Americanus). By R. Hunt, A. Bookman and M. J. Tierney. Reprinted from the Centralblatt für Physiologie, xi, 1897.

On the nature of the cardio-pneumatic movements. By S. J. Meltzer. Reprinted from the American Journal of Physiology, i, 1898.

Contributions to the physiology of the cardiac nerves in the guinea-pig. By D. W. Harrington. Reprinted from the American Journal of Physiology, i, 1898.

The restoration of coordinated, volitional movement after nerve "crossing." By R. H. Cunningham. Reprinted from the American Journal of Physiology, i, 1898.

The cortical motor centres of the opossum (Didelphys Virginiana). By R. H. Cunningham. Reprinted from the Journal of Physiology, xxii, 1898.

On the paths of absorption from the peritoneal cavity. By S. J. Meltzer. Reprinted from the Journal of Physiology, xxii, 1898.

Physiological experiments with intestinal irrigation on pulse tension, temperature, renal secretion, and intestinal absorption. By R. C. Kemp. Reprinted from the New York Medical Journal, lxvii, 1898.

The functions of the ear and the lateral line in fishes. By Frederic S. Lee. Reprinted in the American Journal of Physiology, i, 1898.

Reprint from American Journal of the Medical Sciences. January, 1887.

IS THE "KNEE-JERK" A REFLEX ACT?

A RESEARCH MADE AT THE PHYSIOLOGICAL LABORATORY OF THE COLLEGE OF PHYSICIANS AND SURGEONS, NEW YORK.

By Warren P. Lombard, M.D.

The experiments here recorded were made in the Physiological Laboratory of the College of Physicians and Surgeons. I take this opportunity to express my thanks to Dr. John G. Curtis for his kind advice and assistance.

Character and Results of the Experiments.

The object of the research described in this paper was to determine whether the time between the moment of the blow on the ligamentum patellæ and the beginning of the following contraction of the quadriceps muscle, is long enough to permit the phenomenon to be a reflex act. The result was the discovery that this period was only about one-fourth as long as that required for a skin reflex from the knee, and very little longer than that seen when the quadriceps muscle is incited to action by direct electrical stimulation.

Current Theories.

Since 1875, when the attention of physicians was first called to the diagnostic importance of the phenomenon known as "knee phenomenon," "patella-tendon reflex," "knee-jerk," "knee-kick," "myotatic contraction," etc., there has been much thought given to the subject. The literature is already considerable. I have beside me over a hundred references, and there are undoubtedly many more. It would seem that there could be little new to say, but, in truth, all this work has not definitely determined the nature of the process, and it is not known today whether it is a reflex action or not.

There are two leading views concerning the matter; the one regards the contraction of the quadriceps muscle which follows a

blow on the ligamentum patellæ as a reflex act, the other considers that it is due to mechanical stimulation of the muscle fibres. It has also been proved by experiments that the organ stimulated is, under normal conditions, not in the skin and not in the part of the tendon struck, but that it is situated at a distance, and is simulated by the sudden twitch and by the vibrations of the tendon, resulting from the blow. The nerve fibres which have been discovered in in the tendon, near its attachment to the muscle, and in the sheath and the intestinal tissue of the muscle, as well as the muscle fibres themselves, are capable of being excited to action by mechanical stimuli, and they both seem to be in position to be affected by any sudden jerk or vibration of the tendon. Which of these organs is stimulated? If it be the afferent nerve fibres, the action is reflex; if it be the efferent nerve fibres or the muscle fibres, it is a local phenomenon. Both those who regard the knee-kick as a reflex act and those who consider it an entirely muscular operation admit that the integrity of the reflex arc is necessary to the phenomenon, for this has been proved by physiological experimentation as well as by clinical and pathological observations.

The chief argument in favor of the reflex idea is simply that the undoubted influence of the cord over the phenomenon can be satisfactorily explained in no other way. An explanation is given, however, by those who consider the process to be entirely muscular. They claim that the irritability of the muscle to mechanical stimuli is dependent on the tonus of the muscle, and that this condition is dependent on a continuous shower of weak reflex impulses from the cord. The loss of any part of the reflex arc is followed by a loss of muscle tonus, and, consequently, by a loss of the "knee-kick." The strength of this theory is somewhat impaired by the fact that we know little or nothing concerning muscle tonus, and that some observers state that it is not to be discovered by the most careful methods of experimentation.

The great argument advanced against the theory that the "knee-kick" is a reflex act, is based on experiments which are thought to show that the time elapsing between the moment of the blow on the ligament and the beginning of the contraction of the quadriceps muscle is too short for a reflex action. Thus the majority of observers find the interval to vary between 0.030 second and 0.040 second, except under abnormal conditions, when, in lateral sclerosis, for example, it has been found as short as 0.016 second. Such intervals of time are compared with the presumable time, and are found to be three times as short as they should be were the action a reflex process.

The reflex time for such as act an the "knee-kick" is, unfortunately, unknown and has to be calculated. Thus, it is said that the whole reflex time is the sum of: 1. The time required for the transmission of the nerve impulse through the afferent and efferent

nerves (a distance of 1½ metres at the rate of 30 metres a second), 0.045 second; 2. The time occupied by the reflex processes within the spinal cord (according to Exner's determinations from experiments on winking), 0.055 second; and 3. The latent period of the muscle (determined on frog's muscle), 0.010 second. The whole reflex time is, therefore, said to equal about 0.110 second, while the interval between the blow and the contraction of the quadriceps equals only 0.030–0.040 second.

The champions of the reflex theory can scarcely doubt the accuracy of the experiments in which so many competent observers have gained the same results, but they answer that the time of such a reflex act as the "tendon reflex" may well be much more rapid than that which has been calculated. Thus, some observers have stated the rate of transmission of nerve force at 90 metres a second, instead of 30 metres, the assumed rate. The time Exner found for winking may not at all apply to processes in the lumbar cord. One has no right to judge the latent period of man's muscle from that of frog's muscle. In fact, there is no proof that the "tendon reflex" is not a very rapid reflex act.

And thus the question is left undecided, neither party being able to advance any absolutely conclusive argument.

Experiments by the Author.

Study of the work already done on this subject led me to think that it was quite possible that the contraction of the quadriceps muscle following a blow on the ligamentum patellæ was a compound act; that both sensory nerve fibres and muscular fibres were stimulated by the twitch; and that the contraction was due, first, to direct mechanical stimulation of the muscle fibres, and, second, to reflex nerve impulses. This might well be the case, and yet the two movements might be so fused together that the unaided eye would be unable to distinguish them. The idea naturally suggested itself, that, by the graphic method, one might get a curve which would reveal the influence of two separate impulses. Moreover, one could measure the intervals of time elapsing between the moment that the blow was struck and the instant that each of the waves of contraction, resulting from the two impulses, should begin to show itself, and could compare these intervals with the period elapsing before the contraction of the muscle when it was stimulated directly by an induction current, or, reflexly, by an impulse coming from the skin near the knee. If when the ligamentum patellæ was struck, two oscillations of the curve of contraction should be seen, and two intervals should be obtained which corresponded, the one, with those got when the muscle was stimulated by electricity, and the other, with those got when the muscle was stimulated by reflex impulses, the cause of the

contraction would be evident. If, on the other hand, no second interval should be seen, it would be no proof that the act was a simple one; but the time elapsing before the beginning of the contraction might be found to correspond to one or the other of these periods, and at least the true nature of the beginning of the phenomenon might thus be disclosed.

Accordingly, a number of experiments were made, in which the moment when the stimulus was applied and the moment when the quadriceps muscle had contracted sufficiently to move the foot were accurately recorded. The stimulus was applied in three different ways, viz.: 1. Directly to the muscle, by an induction current sent into it through the skin; 2. Indirectly, by a blow on the ligamentum patellæ; and, 3. Reflexly, by means of irritants employed on the skin near the knee. A study of the form of the curves and of the intervals of time thus obtained gave the following results.

Under normal conditions, when the ligamentum patellæ is struck, the curve of the resulting contraction of the quadriceps muscle shows an unbroken rise, followed by an equally regular fall, and presents no peculiarity which would suggest that the muscle had received more than one stimulation.

The shortest interval between the moment of stimulation and the beginning of the contraction, as registered by the movement of the foot, is seen when the muscle is stimulated directly by the induction current; the next shortest, when it is stimulated by a blow on the ligamentum patellæ; and the longest, when it is stimulated by a reflex impulse coming from the skin near the knee. The time determinations of these intervals were gained in each case by the same apparatus, and can, therefore, be safely compared.

The following table shows the percentage in which an interval of any given length occurred in the experiments of each day, and in the total number of experiments, made with each of the three methods of stimulation. Under Series I. are grouped all that series of experiments in which the rectus was stimulated directly by electricity; Under Series II. are grouped those experiments in which the stimulus was a blow on the ligamentum patellæ; and under Series III. are grouped those experiments in which the muscle was stimulated by a reflex impulse from the skin near the knee. The experiments of different days are placed in separate columns, and the letter beneath the date represents the name of the man experimented on. At the left hand of the table, beneath the word seconds, is a column of intervals seen to elapse between the moment the stimulant was applied and the moment the foot began to be moved by the contracting quadriceps muscle. On the same line with each interval is seen the percentage of the experiments of each day in which that interval occurred; and at the right hand of the table, under I., II., III., stand the percentages of all the experiments having this interval by each of the three methods.

Table of Percentages, etc., January and February, 1886.

Seconds.	Series I.								Series II.					Series III.					Total.		
	Feb. 5.	Feb. 8.	Feb. 9.	Feb. 23.	Feb. 25.	Jan. 21.	Jan. 26.	Feb. 5.	Feb. 6.	Feb. 8.	Feb. 9.	Feb. 23.	Feb. 25.	Jan. 26.	Feb. 8.	Feb. 9.	Feb. 23.	Feb. 25.	I.	II.	III.
	A.	B.	C.	D.	D.	A.	B.	A.	D.	B.	C.	D.	D.	B.	B.	C.	D.	D.	A, B, C, and D.	A, B, C, and D.	B, C, and D.
0.03 0.04	...	...	9	...	...	...	...	...	...	...	...	...	7	...	...	...	...	...	1.6	0.9	
0.04 0.05	...	6	...	...	...	29	9	...	...	11	9	...	43	...	...	...	...	...	1.6	12.3	
0.05 0.06	20	40	27	30	13	71	9	60	...	...	4	...	36	...	...	...	...	...	26.2	17.5	
0.06 0.07	40	20	46	50	80	...	9	20	...	11	18	7	7	...	...	...	...	...	47.5	8.8	
0.07 0.08	30	20	9	20	7	...	55	20	63	33	23	39	...	...	...	...	...	...	16.5	28.1	
0.08 0.09	10	7	9	...	...	...	9	...	37	23	27	35	7	...	...	...	...	...	4.9	20.9	
0.09 0.10	...	...	...	...	...	...	...	...	...	...	5	16	...	...	...	...	...	...	.....	5.3	
0.10 0.15	...	7	...	...	...	...	9	...	...	11	14	3	...	...	8	...	...	...	1.6	5.3	2.1
0.15 0.20	...	...	...	...	...	...	...	...	...	11	...	...	...	16	25	...	...	8	.....	0.9	10.4
0.20 0.25	...	...	...	...	...	...	...	...	...	...	...	...	...	17	42	34	34	75	.....	.....	43.7
0.25 0.30	...	...	...	...	...	...	...	...	...	...	...	...	...	17	...	33	33	17	.....	.....	18.7
0.30 0.35	...	...	...	...	...	...	...	...	...	...	...	...	...	50	17	33	33	...	.....	.....	22.9
0.35	...	...	...	...	...	...	...	...	...	...	...	...	...	...	8	...	...	...	.....	.....	2.1
No. of experiments.	10	15	11	10	15	14	11	5	8	9	22	31	14	6	12	9	9	12	61	114	48
Average interval	0.068	0.067	0.061	0.063	0.063	0.052	0.075	0.060	0.079	0.090	0.077	0.082	0.051	0.271	0.232	0.268	0.270	0.226	0.064	0.071	0.253

At the bottom of the table are two lines of figures arranged by series and dates. The upper line gives the number of experiments made on each day by each method of irritation, and also the total number of experiments made with each method of irritation. The lower line gives the average length of the intervals obtained from these experiments.

A glance at this table shows a great similarity in the length of the intervals in the experiments of Series I. and Series II., whilst the intervals of the experiments of Series III. are all very much longer than these. A comparison of the lengths of the average intervals got from experiments in Series I. and II.—*i. e.*, from experiments in which the muscle was stimulated by the direct application of electricity, and those in which it was stimulated by a blow on the ligamentum patellæ—reveals a difference of only 0.007 second. This similarity suggests a similarity in the phenomena. Comparison of these average intervals with the average interval of experiments in Series III.—that is, those in which the muscle was stimulated by a reflex impulse from the skin—discloses the fact that the average interval for experiments in Series III. is three to four times as long as the average intervals of experiments in Series I. and II.

How far may these average intervals be trusted for purposes of comparison? In all experiments marked variations in the length of the intervals were seen. They were least when the muscle was stimulated by electricity, more when the stimulant was a blow on the ligamentum patellæ, and by far the greatest when the stimulus was of reflex origin.

When the muscle was excited to contraction by direct electric stimulation, the average length of the intervals obtained from the experiments of each day was between 0.060 second and 0.070 second; the length of the average interval got from all the experiments was 0.064 second; and 47.5 per cent. of all the experiments had intervals ranging between 0.060 second and 0.070 second. Outside of these limits the variations were as follows: 29.4 per cent. had shorter, and 23 per cent. had longer intervals. These figures make it evident that 0.064 second is a just average interval.

When the muscle was stimulated by a blow delivered on the ligamentum patellæ, the average length of the intervals obtained from the experiments of each day varied from 0.050-0.090 second; the length of the average interval got from all the experiments was 0.071 second; and 36.9 per cent. of all the experiments had intervals ranging from 0.060-0.080 second; 30.7 per cent. had shorter, and 32.4 per cent. had longer intervals. Thus, though one must remember that the intervals varied widely, one can fairly state the average interval at 0.071 second.

Similarly, it may be said that the average interval obtained from experiments in Series III. may fairly be accepted for purposes of comparison.

Before any conclusion as to the similarity or dissimilarity of these phenomena can be based on a comparison of their average intervals, one must ascertain upon what the differences in the average intervals depend. An analysis of the interval recorded as elapsing between the moment that the stimulus was applied and the moment the foot began to move in response to the contraction of the quadriceps muscle, shows that it is made up of the following periods., viz:

1. The time occupied by all the processes occurring between the moment the stimulant is applied and the moment the stimulus reaches the muscle. This period would vary with each form of stimulant, and would depend on the length and the nature of the path which the stimulus had to travel.

2. The time required for the muscle to respond to the stimulus. The latest observations state the latent period of the normal frog's muscle at about 0.003 second. We do not know the latent period of man's muscle. It would, without doubt, vary with the irritability of the muscle. As in these experiments the subjects were normal and were placed under the same conditions, the latent period of the muscle can be regarded the same in all the experiments.

3. The time required for the muscle to contract enough to move the foot. This would depend on—

a. The tension of the muscle at the time it was irritated. This was very slight and was apparently the same in all the experiments.

b. The amount the contracting muscle was stretched by the resistance of the leg, etc. This was the same in all experiments.

c. The time required for the contracting muscle to overcome the inertia of the limb and of the recording apparatus. This would be, probably, about the same as the time required to register the jar of the blow. This period was determined by fifty experiments to be about 0.013 second. It was about the same in all experiments.

d. The number of muscle fibres irritated, which would vary with the nature of the stimulant, its strength, and the method of its application.

e. The strength of the stimulus.

4. All intervals recorded are 0.003 second too short, for this amount of time was lost by the electro-magnet in recording the moment of the blow.

The periods numbered 2, 4, and *a*, *b*, and *c*, under 3, were the same for all forms of experiments and need not be further considered. Any differences seen between the average intervals obtained by the three different methods of experimentation were dependent on differences in the length and nature of the paths which the stimulus had to travel; on differences in the number of muscle fibres stimulated, due to differences in the nature, strength, and method of application of the stimulant; and on differences in the strength of the stimulus.

How far would those causes which determine the activity of the

contraction of the muscle affect the result? In the case of the experiments in which the muscle was stimulated by electricity, the electrodes were only six inches apart, and, therefore, comparatively few muscle fibres were directly stimulated; the stimulus may have spread to many others, however, by means of the nerves which were excited. The stimulant employed was of medium strength, an induction current being chosen which just sufficed to cause an undoubted movement of the foot. These facts would lead one to surmise that a comparatively long time elapsed between the moment that the stimulus reached the muscle and the moment the foot began to move in response to its contraction.

In the case of experiments in which the muscle was stimulated by the results of a blow on the ligamentum patellæ, if the stimulation was reflex, all the muscle fibres must have been stimulated in each experiment; if stimulation was effected by direct excitation of the muscle fibres, the number of fibres stimulated must have varied with the tension of the muscle, the force of the blow, and the place struck. The strength of the stimulus, though undoubtedly very variable, was, to judge from the extent of the movement of the foot, in most experiments, considerable. These facts lead one to believe that a comparatively short time elapsed between the moment that the stimulus reached the muscle and the moment the foot began to move in response to its contraction.

There is no way of accurately determining how many muscle fibres were stimulated by either method of experimentation, or what was the relative strength of the stimulants employed. The above facts, however, would lead one to infer that the contraction of the muscle would have been comparatively slow in experiments in which the muscle was stimulated by electricity, and, so far as this influence could have determined the result, that the average interval would have been somewhat longer in these experiments than in those in which the muscle was stimulated by the results of a blow on the ligamentum patellæ. In reality, however, the reverse was true, and the average interval of experiments in Series I. was 0.007 second shorter than that of experiments in Series II. This result can be due only to the other factor which goes to determine the length of the intervals—that is, the length and the nature of the paths which the stimulus had to travel in the two cases. The stimulus has, then, to pass by a longer path in the case of experiments in which the ligamentum patellæ is struck than in the case of those in which the quadriceps is stimulated by electricity; and this difference in the length and nature of the paths is enough to make the average interval of the experiments of Series II. not only as long, but 0.007 second longer than that of the experiments of Series I. As has been said, there is no way of determining what effect the possible difference in the number of muscle fibres stimulated by the two methods of experimentation, and the possible difference in the strength of the

stimulant employed in the two cases, may have had on the average intervals; one can only conclude that the difference in the length and nature of the paths travelled in the two cases is somewhat more than is represented by 0.007 second.

What are the paths which the stimulus would have to pass over when the two methods of stimulation under consideration are employed? In the case of electric stimulation the electricity would only have to pass from the wet electrode, through the moist skin, the subcutaneous tissue, and the fascia to reach the muscle. In the case of a blow on the ligamentum patellæ, if the muscle fibres were stimulated mechanically, the jerk and the vibrations of the ligament would have to be transmitted along the chain of ligament, patella, quadriceps tendon, and quadriceps muscle. If the muscle were stimulated reflexly, the stimulus would have to pass, in addition to the above, through the afferent nerves to the spinal cord, through the reflex mechanisms in the cord, and through the efferent nerves to the muscle. There can be little doubt as to which path the stimulus would soonest reach the muscle. The muscle would be stimulated soonest by electricity, almost as soon by the mechanical stimulation of a sudden jerk transmitted to it from the tendon, and some time later by reflex stimulation.

The difference between the periods of time required for the stimulus to pass from the point to which the stimulant was applied, to the muscle, in the experiments of Series I. and II., is, as has been stated, somewhat more than 0.007 second. Were the stimulation reflex in character, we should expect a very marked difference. The reflex time for such a process as the "knee-kick" has been supposed to be, cannot be calculated, because the rapidity of different reflex processes probably varies greatly; we may, however, obtain a rough idea of its length. It is the sum of the following periods, viz.:

1. The time required for the transmission of jerk and vibration, resulting from the blow, from the ligament to the sensory nerve ends in the tendon or muscle, and the time spent by them in awakening to activity. This period cannot be determined.

2. The time required for the transmission of the stimulus through the afferent nerves to the cord, and from the cord through the efferent nerves to the muscles. At the quickest estimated rate of transmission of nerve force, 90 metres a second, 0.016 second would be required for the passage of the impulse through a metre and a half of nerve length. Exner, in his calculations, uses the rate of 62 metres a second; at this rate 0.024 second would be required. By the more usual estimate, of 30 metres a second, nearly 0.050 second would be required for the transmission of the impulse to and from the cord.

3. The time occupied by reflex processes within the cord is probably very variable. Exner found it, in his determinations on winking, to equal 0.055 second.

4. The latent period of the muscle.

It is not worth while to add these periods together, for the result would give no accurate idea of the reflex time. The only use of referring to them is to show that, so far as we can judge from present knowledge, even rapid reflex processes require considerable time. Here it is interesting to compare the average intervals got by the experiments of Series I. and II. with the average interval of experiments of Series III., in which the stimulus was a reflex impulse called out by a vigorous electric irritation of the skin near the knee The average interval of the experiments in Series I. is 0.064 second, that of the experiments in Series II. is 0.071 second, and that of the experiments in Series III. is 0.253 second—*i. e.*, the average interval of the experiments in which the muscle was stimulated by a reflex impulse from the skin near the knee is three or four times as long as that of the experiments in which the muscle was stimulated by electricity, or by a blow on the ligamentum patellæ. The fact that a portion of the reflex interval was occupied by a summation of the impulses produced by the induction shocks, makes little difference, for, as the current was quite strong, and the hammer of the induction apparatus was vibrating very rapidly, the summation would have occupied but little time.

It may well be said that a reflex process, such as the "tendon reflex" is supposed to be, might be very much shorter than that of a skin reflex from the knee. This is true, but that it might be so much shorter as to require but little more time than the direct electric stimulation of the quadriceps is not at all evident. On the other hand, the difference found between the average intervals of experiments in Series I. and II. is about what one would expect to find were the muscular fibres of the quadriceps stimulated mechanically by the jerk and vibrations which would result from the blow on the ligamentum patellæ.

There is one more point to which it is necessary to refer. Not only do the experiments in Series II. have intervals closely resembling those of the experiments in Series I., but a larger percentage of the experiments of Series II. have very short intervals than of the experiments in Series I. Thus, 12.3 per cent. of the experiments in Series II. had intervals ranging from 0.040–0.050 second, while only 3.2 per cent. of the experiments of Series I. had intervals as short. These very short intervals of Series II. are hard to reconcile with the idea that the stimulus had to pass through the cord before it reached the quadriceps muscle, but they might well have occurred had a vigorous blow on the ligament thrown all the muscle fibres into vibration.

The results of my experiments do not settle the question in dispute, but they add weight to the opinion already expressed by many competent observers, that the "knee-kick" is not a reflex act. Moreover, the mechanical conditions on which the "knee phenome-

non" depends, the fact that muscle fibres are stimulated if they are suddenly twitched, and that the fibres of the quadriceps are in a position to be thus stimulated, and the time found to elapse between the blow on the ligamentum patellæ and the contraction of the quadriceps, all go to suggest that the phenomenon is entirely peripheral.

Although, as a rule, the contraction of the quadriceps which follows a blow on the ligamentum patellæ is a simple act, there was one set of experiments, among those recorded, which seemed to be an exception. Many of the curves got from one man, and on one day, showed an irregularity such as one might expect, if, when the original contraction of the muscle had reached its highest point, or when the muscle had even begun to relax, a second impulse had reached it, and caused it to contract still further. What was most interesting in this change in the form of the curve was that it occurred at an interval after the blow which closely corresponded to the interval got when the muscle was stimulated by a reflex stimulus coming from the skin near the knee. It suggested, of course, that the muscle received two impulses, as a result of the blow on the ligamentum patellæ, the one, a direct mechanical stimulation, the other, a reflex stimulus. The curve was never carried by the second oscillation to any marked height, however, and the chief part, as well as the first part of the "knee-kick," under normal conditions, at least, would seem not to be due to reflex stimulation. The rest of the curves obtained from the same man, on other days, and from the other men experimented upon, were searched in vain for any wave which might suggest the action of two separate impulses. The fact that such an oscillation of the curve was noticed is the more interesting because I have heard that de Watteville claims that the "knee-kick" is always a compound act.

As the results here given are of importance, and are liable to be questioned, it seems desirable that a more detailed account of the experiments and of the methods pursued should be given. I therefore state them here for those readers who are more especially interested in this subject.

Requirements of the Research.

The experiments must be made on man.

The subject must be placed at rest, in an absolutely comfortable position, in order that there shall be no disturbing movements or unwished-for reinforcements.[1]

The thigh must be steadied by a form of support which, while it prevents movement being caused by the jar of the blow, when the

[1] Mitchell, The Medical News, February 13 and 20, 1886.

ligamentum patellæ is struck, does not press on the quadriceps muscle, or on the large vessels or nerves.

The leg must be entirely free to move in response to the contraction of the quadriceps, and the weight of the leg and foot must be as far as possible gotten rid of, in order that the muscle may not be stretched, and the beginning of the contraction be lost. The contraction, rather than the swelling of the muscle, must be recorded, because it is the more marked event, and more likely to reveal the character of the action.

The recording apparatus must consist of a rapidly moving surface, and of three writing points: one attached to a tuning-fork to record the rate at which the surface is moving; another, connected with an electro-magnet, to mark the moment the irritation is given; and a third, to write the contraction of the muscle.

In accordance with these requirements, the following apparatus was put together.

Description of the Apparatus Used in the Experiments.

The man experimented upon lay on his left side on a comfortable couch, so formed as to support the head and back. The right thigh rested on a prop of plaster, shaped so as to conform to the inner and posterior surface of the thigh, and of such a height as to hold the knee on a level with the hip-joint. The right foot was supported by a swing suspended by a cord from the ceiling.

The movement of the foot, in response to the contraction of the quadriceps, was recorded as follows: A strong inelastic thread, attached by one end to the swing on which the foot was fastened, was guided by two accurately working pulleys to the top of the recording needle. One of these pulleys was on a movable stand, having a heavy base, and its position could be changed to correspond to the position of the foot, and thus the direction and the tension of the thread could be regulated. The other pulley held a fixed position, and the thread passing over it suspended the writing mechanism. This mechanism was cross-shaped, and consisted of a vertical shaft bearing a horizontal needle, which was adjustable at any desired height on the shaft. The vertical shaft was suspended from the end of the thread beneath the second pulley, and was insured free vertical movement and freedom from lateral oscillations by passing through two smoothly bored holes in two thin strips of metal, which were supported about fifteen centimetres apart by an iron standard. One end of the horizontal needle terminated in a fine rounded point, and rested against the blackened drum of a Ludwig kymographion (Baltzer's manufacture). Constant contact with the drum was secured by a fine plumb line, which hung against the

other end of the needle. Contraction of the quadriceps and extension of the knee caused the needle to rise, while relaxation of the muscle and flexion of the knee were recorded by a fall of the curve. It was desired to detect any irregularity in the contraction of the quadriceps, and, therefore, it was especially necessary to prevent the needle from being thrown by the sudden jerk of the kick beyond the height which corresponded to the absolute movement of the foot. A thin yielding band of rubber was therefore attached to the lower end of the vertical shaft and to the floor.

The kymographion ran with great regularity, but with was not relied upon, and the rate of rotation was measured during each experiment by a tuning-fork, which, by means of a light metal point attached to one of the arms, wrote its vibrations on the drum.

An electro-magnet recorded, by a light lever attached to its armature, the moment the blow was struck on the ligamentum patellæ, or the moment that the induction current was thrown into the quadriceps muscle or the skin. The pattern of the magnet resembles that of Pfeil, of Berlin (described by Tigerstedt, *Arch. für. Phys.*, Supplement Band, 1885), and its latent period was a little less than 0.003 second.

The instruments used for irritating were as follows:

The blow on the ligamentum patellæ was given by a medium-sized steel hammer, one end of the head of which was tapered to a dull edge, about an inch long and covered with a rounded rubber cap, of the thickness of a lead pencil. In cases in which the "knee-kick" was well marked, the ordinary percussion hammer was sufficient. The electric circuit of the recording electro-magnet was closed when a strip of platinum foil on the rubber end of the hammer touched a piece of gold braid, which was fastened by a garter over the ligamentum patellæ.

The induction current was applied to the rectus muscle by two wet electrodes, placed on the skin over the middle third of the muscle and about six inches apart. When it was necessary to stimulate the cutaneous nerves, the induction current was applied by a wire brush and a platinum point about half an inch apart.

In the case of electrical stimulation, one key simultaneously closed two circuits; the one going through the muscle, or the skin, the other through the electro-magnet.

A Grove cell was used for the electro-magnet, and another for the Du Bois-Reymond induction coil.

The same magnet recorded the moment of stimulation, and the same apparatus wrote the beginning of the contraction of the quadriceps, whatever the means of stimulation employed—*i. e.*, whether the muscle was stimulated by a blow on the ligamentum patellæ, by the direct application of the induction current, or by the reflex impulse resulting from the irritation of the skin near the knee. Therefore, the latent period for the apparatus was the same in all

the experiments, and any difference in time which was found, was due to variations occurring between the moment the stimulant was applied and the moment the stimulated muscle had contracted enough to move the foot; in other words, to differences in the length and nature of the paths which the stimulus had to travel, and in the activity of the muscular contraction.

To conclude—from the experiments recorded in this paper, it would seem that the contraction of the quadriceps muscle following a blow on the ligamentum patellæ comes much too soon to be the result of a reflex stimulation. It is probable that the stimulation is due to a sudden stretching of the muscle fibres, and that the stimulus has the same character as when the muscle receives a direct blow. Before this conclusion can be accepted, however, the undoubted influence of the spinal cord upon the production of the phenomena must be explained. The current explanation that the irritability of the muscle to finer mechanical stimuli is dependent on "muscle tonus," will not be altogether satisfactory until the existence of "muscle tonus" is proved.

It seems probable, that, in addition to the first impulse which comes to the quadriceps when the ligamentum patellæ is struck, occasionally a second impulse, of reflex nature, originating either in the nerve ends of the skin or of the tendon and muscle, may come to it and increase the height of the contraction. Under normal conditions, however, this would seem to play a very subordinate part.

ON THE NATURE OF THE KNEE-JERK.

By WARREN PLIMPTON LOMBARD, M.D., *Assistant in Physiology at the College of Physicians and Surgeons of New York.*

It has long been known that if the ligamentum patellae of a normal individual be struck when the leg is hanging freely in a position of partial flexion, the quadriceps muscle is irritated and contracts, causing a sudden extension of the knee, which we call a knee-jerk. The process by which the muscle is stimulated, however, is still a subject of discussion.

Some authors claim that the muscle fibres are directly stimulated by the sudden twitch to which they are subjected, the method of excitation being similar to that resulting from a direct blow on the muscle, and these writers think that the time which elapses between the moment of the blow on the ligament and the resulting muscular contraction is far too short to admit of any other interpretation.

Other authors call attention to the fact that the phenomenon cannot be obtained if the nerve connecting the muscle with the spinal cord first be severed, or if the corresponding reflex mechanisms of the cord have been injured by disease, and conclude that since the integrity of the reflex arc is essential to the phenomenon the knee-jerk must be a reflex act. They admit that the time involved in the process is very short, but say that the time required by such a reflex action, as they suppose this to be, is not known, and that it may well be as short as the interval found.

Those who regard the process to be wholly peripheral, answer the objection that it is lost if the reflex arc be destroyed, by suggesting that the ability of a muscle to respond to such a slight mechanical stimulus as that caused by a blow on its tendon may depend upon its having a certain amount of tension, and that this necessary tension is dependent on the tonus of the muscle, which is lost, when, upon division of the nerve or destruction of the cord, tonus impulses cease to come to the muscle.

Thus we find two distinct parties; the one regards the phenome-

non reflex, the other considers it a wholly peripheral process. Both admit that the integrity of the reflex arc is essential to the knee-jerk, and that the time involved in the process is much shorter than that required by the few reflex acts of which the time has been studied.

Undoubtedly the reflex theory offers the simplest and most satisfactory explanation of the intimate dependence of the phenomenon upon the spinal cord. Indeed the time argument would have but little weight if those who doubt the reflex nature of the process were unable to explain this connection. It is worth while, therefore, to consider the soundness of their explanation.

As has been said, they assume that the ability of the muscle to respond to the twitch transmitted to it from its ligament is dependent on the tension of the muscle, and that this is dependent on tonus impulses coming to it from the spinal cord.

One cannot help feeling that this explanation has been manufactured to meet the emergency and is somewhat forced, both because of the uncertain basis on which the tonus theory rests, and because there is no proof that the irritability of a muscle to mechanical stimuli is dependent on its tension.

The knee-jerk, though it varies greatly in amount, can almost always be obtained, while there is reason to doubt that muscles are kept continuously in tonus by impulses either of automatic or of reflex origin. It is most probable that there are times when they receive slight motor impulses of reflex nature, and that they respond by the feeble increase in tension which we call tonus, but there is no reason to suppose that they are continually in receipt of tonus impulses.

Suppose, however, for the sake of argument, that tonus is continuous, there is no surety that it is essential to the knee-jerk. It is true that for purely mechanical reasons, tension of the muscle not only favors but is necessary to the phenomenon. If the blow be struck when the ligament and muscle are loose, there is no twitch transmitted to the muscle and consequently no knee-jerk developed. On the other hand, if the slack has been taken up, the sudden strain caused by the blow on the ligament is transmitted through the whole muscle. Moreover, when the muscle is under tension the smallest contraction will reveal itself. By giving the leg a proper position, one can secure to the muscle any desired degree of tension, this, however, does not enable one to get a knee-jerk when the spinal cord is diseased.

If tonus be essential to the phenomenon it would seem to be for some other reason than because it supplies a required tension. One

might conceive that in some unknown way it increases the irritability of muscle tissue. If this be true, however, it would seem as if the knee-jerk which disappears when the tonus of the muscle is lost, upon division of its nerve, it would be obtained again, when, by electrical stimulation of the cut-nerve, the tension of the muscle is restored. This experiment has been made upon a rabbit but failed to recall the knee-jerk.

This last winter I examined a man who was young, vigorous and showed no sign of disease. His legs were well developed, and his muscles firm and elastic. There was no sign of lack of tension of the muscles. He claimed to be the equal of his fellows in all manly sports. I could not prove that he had or had not tonus of the muscles, but I saw no reason to doubt that he had as much as most men. This man gave no knee-jerk and no reenforcement of the knee-jerk.

It is not uncommon to find a person in good health with no knee-jerk, though it is exceptional to find one from whom a reenforced knee-jerk cannot be obtained. If the absence of the knee-jerk in these cases is due to a lack of tonus, and if muscle tonus plays the important rôle attributed to it, it is strange that these men should show no disturbance of muscular coordination. Indeed, such cases tend to show that something more than a suitable condition of the muscles is essential to the production of the knee-jerk.

Any theory of the nature of the knee-jerk, to be acceptable, must likewise explain the reenforcements of the knee-jerk. It occurred to me, therefore, that a study of the reenforcements of the knee-jerk might throw much light on the nature of the phenomenon. If the processes on which the knee-jerk depends are wholly peripheral, the increase of the contraction which results from the reenforcing act must necessarily be due to changes occurring within the peripheral mechanisms. How might the ability of a muscle to respond to a blow on its tendon be increased by a reenforcing action? Two ways suggest themselves, viz.:—

1. The tonus of the muscle might be increased as a result of an increased activity of the spinal centres, which might be caused by the development of a voluntary action, a painful sensation or an active emotion or thought.

2. The irritability of the muscle might be increased in some inscrutable way by the reenforcing process.

I made a careful study of the quadriceps muscle and tried to discover whether it gained in tension or in irritability when the hands were clinched. I found it difficult to construct an apparatus capable

of measuring delicate changes in muscle tension, but finally fixed upon one which answered the requirements fairly well. It recorded the smallest contraction of the quadriceps which I could learn to make voluntarily, and this contraction was so slight that it could not be detected by the eye or by a trained hand placed over the muscle. It seemed as if a smaller increase in tension than this could hardly be regarded as sufficient to influence the ability of the muscle to respond to the blow, either because the tenser muscle fibres would favor the transmission of vibrations, or because, the slack having been taken up, the muscular contraction would reveal itself more readily.

The apparatus used to record the contraction of the quadriceps consisted of a long, light, stiff lever, the axis of which was fastened by an elastic band upon the ligamentum patellae. The lever rested, near its axis, on the lower edge of the patella. When the quadriceps contracted it made the ligament more tense, and at the same time tilted the patella; both of these movements caused the recording end of the lever to descend. The lever magnified the movement of the ligament and patella about twenty times.

The man lay on his back, on a bench made with adjustable segments, which supported the head, back, thighs, legs and feet in any desired degree of flexion. A control lever, which recorded every movement of the head of the tibia, wrote the movements of the knee caused by the respiration, the pulse and jars.

A Marey's tambour, connected with a dynamometer, wrote with its lever the moment that the reenforcing movement of clinching the hands was performed.

Not to go further into details, suffice it to say that no contraction of the quadriceps was seen to follow the most active hand clinch in the case of any of the normal men experimented on, though such an action was very potent in reenforcing the knee-jerk.

There is one experiment which deserves separate mention. The young man in question had no knee-jerk, but showed an active reenforced knee-jerk. It seemed as if in his case, at least, one might find a change in the tension of the quadriceps, i. e., if the knee-jerk which appeared when he reenforced depended on an increase of tonus, but none was found.

From these experiments it would seem that such an act as clinching the hands, though capable of reenforcing the knee-jerk, affects the tension of the quadriceps muscles little, if at all, under normal conditions.

Finding no increase in the tonus of the muscle when the hands were clinched, I proceeded to test the irritability of the muscle at the time that the reenforcing act was being performed. I used as a test, the strength of the induction current required to call out the least contraction which the lever already described was capable of recording. No

increased irritability to electrical stimulation was discovered. It may be said that the irritability of the muscle to mechanical stimuli may, nevertheless, have been enhanced. This seems doubtful, however, for as a rule when the irritabilty of a muscle is increased, it responds more readily to all forms of stimuli.

In short, I was unable to find any evidence that, in the case of normal men, lying at rest, such an act as voluntarily clinching the hands has any effect on either the tension or the irritability of the muscle. This result corresponds with that of Mitchell and Lewis,[1] who found that muscular contractions called out by electricity cannot be reenforced, a result which would be inexplicable in case the reenforcing influence affected the peripheral mechanisms.

If these results are correct, the knee-jerk cannot be a purely peripheral phenomenon and is, probably, in spite of the short time, a reflex process. This conclusion is borne out by the results of experiments which I made at the College of Physicians and Surgeons of New York, during the past winter.

These experiments were made on twenty-five medical students, all of whom were, as far as could be judged, in good health. It is worth mention that they were wholly unfamiliar with the work and they had no idea of what was expected of them.

The apparatus was the same as that employed by me in the experiments reported in the *American Journal of Psychology*, Oct., 1887. It consisted of a couch, on which the subject lay on his left side; a support for the right thigh; a swing for the right foot, suspended by a long cord from the ceiling; a recording needle, which was attached to the right heel, and which by writing the movements of the foot gave a magnified record of the flexion and extension of the knee; and finally a hammer which delivered a blow of constant and known force.

A clear understanding of the results obtained is only to be reached by a careful analysis of the conditions of the experiment. When the subject is placed on the knee-jerk couch with his thigh on the support and his foot in the swing, the knee assumes a position of partial flexion. If the experimentor draws the lower leg forward, so as to increase the extension of the knee, or backward, so as to increase the flexion of the knee, and then release it, the leg swings like a pendulum backwards and forwards for eight or ten times, each oscillation being smaller than the preceding, until the leg becomes quiet in the original

[1] "Physiological Studies of the Knee-jerk, and of the Reactions of Muscle under Mechanical and other Excitants," by S. Weir Mitchell, M.D., and Morris J. Lewis, M.D., *The Medical News of Philadelphia*, Feb. 13 and 20, 1886.

position of rest. What are the forces which determine how much the knee shall be flexed when in the position of rest?

1. The force of gravity, which tends to bring the swing and foot directly under the point of suspension of the swing.

2. The amount of flexion of the hip joint and the consequent degree of tension of the two joint muscles on the front and back of the thigh.

3. The tension of the muscles on the front and back of the thigh dependent on their natural length and elasticity.

4. The contraction of the muscles caused by nervous or other stimuli.

It may seem a contradiction to speak of muscular contraction as one of the conditions which determine the position of the leg when at rest, but, inasmuch as the theory of muscle tonus still holds, it may not be inadmissible.

Most of the forces enumerated act constantly and continuously. If the body and thigh are immovable, the tension of the muscles of the thigh, as far as it is governed by the position of the hip joint, will be uniform; the elasticity of the muscles will undergo but little change during short intervals of time; the influence of the force of gravity will remain the same; therefore, any change of the knee from the position of rest, must be caused by a difference in the amount of contraction of the antagonistic flexors and extensors.

If these muscles were in receipt of tonus impulses which were continuous and constant, their length would undergo no change on this account; if, however, they received irregularly tonus impulses of varying amounts, their length would change frequently. I was curious to find whether such variations actually occurred, but in the few experiments which I made, I could not discover that the knee moved at all from the position of rest when the subject was calm and was lying quietly.

Now what happens when the ligamentum patellae is struck? The blow is immediately responded to by a contraction of the muscles on the front of the thigh, the knee is extended, and the foot is swung forward. As the extensor muscles cease to contract, the elasticity of the flexor muscles together with the force of gravity cause the foot to swing back; the force of the backward swing is sufficient to carry the foot beyond the position of rest and to flex the knee, though not as greatly as the contraction of the muscles had extended it; this flexion of the knee is in turn followed by extension, and this by a second movement of flexion, and so on, each act being less than the preceding,

until after eight or ten oscillations the knee becomes quiet in the position of rest.

Such is the ordinary sequence of events following a blow on the ligamentum patellae, and, when the subject is in a placid condition, the knee actually returns to the original position of rest time after time, as often as the experiments are repeated. This is illustrated by experiments on S, recorded in Table I., during which the knee invariably returned to the original position of rest.

Description of Table I.

The table is to be read from left to right. In the first column is the number of the observation; in the second, the extent of the knee-jerk or first movement of extension; in the third, the first backward oscillation of flexion; in the fourth, the second oscillation of extension; in the fifth, the second oscillation of flexion; while in the sixth column is recorded the change in the position of the line of rest from that which it occupied before the blow was struck. In this, as in all succeeding tables, the sign + signifies a movement in the direction of extension, recorded in the charts as an upward movement, while the sign — indicates a movement of flexion, recorded in the charts as a downward movement. The figures give the extent of the movement in millimetres. The measurements were all made from the line of rest which was drawn just before the blow was struck.

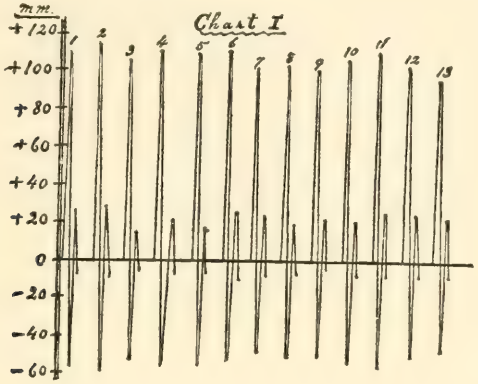
TABLE I.

S, Curve 31.

No. of Observation	1st Extension or Knee-jerk	1st Flexion —	2d Extension +	2d Flexion —	Change of Position of Line of Rest
1	110	55	26	7	0
2	113	58	28	9	0
3	105	52	15	5	0
4	111	56	21	7	0
5	109	55	18	6	0
6	111	55	27	9	0
7	102	49	24	7	0
8	103	50	20	6	0
9	101	50	23	6	0
10	106	53	21	7	0
11	110	55	25	8	0
12	103	51	24	8	0
13	96	46	21	7	0
14	103	51	21	?	0
15	105	52	20	?	0
16	84	43	18	7	0
17	83	42	20	7	0
18	92	45	22	8	0
19	103	52	25	9	0
20	96	48	25	8	0
21	95	47	24	8	0
22	84	39	19	7	0
23	88	43	21	7	0
24	99	50	26	9	0
25	92	45	23	7	0
26	95	48	25	?	0
27	92	46	22	8	0
28	99	51	27	9	0
29	106	53	30	10	0
30	108	55	30	10	0
31	111	56	31	10	0
32	98	46	22	6	0
Average	100	50	23	8	

The regularity of the oscillations is well shown in Chart I., which was constructed from the same curves as this table. The extent of the movements has been reduced three-fourths, which necessitated the omission of the final small oscillations.

S, Curve 31.



As has been said, it is usual for the knee to return to the original position of rest when the subject is in a tranquil frame of mind. When, however, the subject is excited, it is much more common to see the knee become quiet in a different position, and be either more extended or more flexed than before the blow was struck. This is illustrated by the measurements given in the following Table.

Description of Table II.

In this table are collected the changes in the position of the line of rest which occurred in experiments on seven different men. The observations are arranged in columns. At the head of each column is the letter which stands for the subject, and beneath this is the number of another table in this paper, in which the same results are given. Below this heading are recorded the successive changes in the position of the line of rest. The measurements are given in millimetres, and each was made with reference to the position of the line of rest at the end of the preceding observation. The sign + shows that the variation was in the direction of extension, and the sign — that it was in the direction of flexion.

TABLE II.

SUBJECT	A	G	X	D	C	L	U	C	A
No. of Table	I	V	V	V	V	VI	VI	VII	IX
1	0	0	0	+2	+2	+ 2	− 2	+ 5	− 4
Changes in the position of the line of Rest seen to follow the successive Knee-jerks 2	0	0	0	+2	0	+ 1	− 3	− 1	− 5
3	0	0	0	+1	+1	− 6	+ 1	+11	+ 5
4	0	0	0	0	+2	− 5	+ 7	+ 2	− 5
5	0	0	0	+1	0	+ 1	+ 2	+ 7	+ 5
6	0	0	0	0	0	+ 6	− 7	− 5	− 7
7	0	0	0	0	0	+ 4	− 4	+ 2	+ 1
8	0	0	0	0	0	− 1	− 7	− 1	+ 8
9	0	0	0	0	−1	+ 1	+ 6	0	+11
10	0	0	0	0	+1	+ 6	+ 4	0	+ 7
11	0	0	0	0	0	− 1	+ 2	0	−18
12	0	0	0	0	+1	+ 1	− 1	+25	+ 7
13	0	0	0	0	0	− 1	+ 8	+ 5	− 1
14	0	0	0	0	−1	?	+15	+ 2	0
15	0	0	0	0	0	*	+ 6		+ 1
16	0	0	0	0	+1	+ 2	+ 4		?
17	0	0	0	0	0	+ 1	*		*
18	0	0	0	0	0	+ 2	− 3		− 5
19	0	0	0	0	0	+13	+ 3		− 8
20	0	0	0	0	0	+ 1			0
21	0	0	0	0	+1	− 9			− 3
22	0		0	0	0	+18			+ 5
23	0		0	0	0	− 1			+12
24	0		0	0					+ 2
25	0			0					− 5
26	0								

* Break in curve.

During the examinations which are recorded in the first five columns there was little or no change of the position of the line of rest, while during the examinations reported in the last four columns considerable variations occurred. It was noticed that in all the cases in which marked changes in the position of the line of rest appeared, the men were in an excitable condition. Almost all the men were slightly disturbed by the first examination. In the case of A and C the records which show the greatest variations were those obtained the first time they were examined, while the records which show no variations were gained at a subsequent examination.

It is evident then that the knee may return after each knee-jerk to the position held before the blow was struck, or that it may come to rest in a new position, which may be more flexed or more extended than before the knee-jerk was called out. As has been shown such changes in position can only result from an alteration of the tension of the flexor and extensor muscles of the knee, and that this was really the cause of the change of position will become still more evident when we study the relative size of the oscillations which followed the knee-jerk.

Omitting for the present the causes for the varying degrees of tension found, let us see what effect they exerted upon the extent of the knee-jerk. It is to be remembered that the fact that the spinal cord is essential to the development of the knee-jerk is explained by those who disbelieve that it is a reflex act, on the ground that the spinal cord is indispensable to the tonus of the muscle, and that the muscle must have a certain amount of tension in order to be able to respond to blows on its tendon. If it be true that the irritability of a muscle to mechanical stimuli is dependent on its tension, it would seem that the extent of the knee-jerk would vary with the degree of tension of the muscle. In the experiments recorded there is no lack of changes of tension of the muscle or of variations in the size of the knee-jerk, but the degree of tension and the size of the knee-jerk are entirely independent of one another. The truth of this statement is proved by the following table, in which the changes in the tension of the muscles as determined by the variations of the position of the line of rest are recorded side by side with the height of the knee-jerk which was called out immediately after this change of tension.

Description of Table III.

The table is headed by the letters which represent the names of the subjects examined, and beneath each of them is the number of another table of this paper in which these same results appear. Below each letter the results of the examination are arranged in two parallel columns. In the first is recorded in millimetres the variations in the position of the line of rest which occurred in the succeeding observations, the sign + indicating a movement towards extension and the sign — towards flexion. In the second column is stated the extent of the knee-jerks which were called out when the muscles had the tension recorded on the same line in the first column.

TABLE III.

A		C		L		U		U	
IX		VII		VI		VI		(Curve 61)	
Line of Rest	Knee-jerk	Line of Rest	Knee-jerk	Line of Rest	Knee-jerk	Line of Rest	Knee-jerk	Line of Rest	Knee-jerk
0	81	0	63	0	−102	0	81	0	55
− 4	70	+ 5	56	+ 2	59	− 2	60	− 4	48
− 5	50	− 1	60	+ 1	51	− 3	71	+10	51
+ 5	56	+11	61	− 6	68	+ 1	77	+ 7	66
− 5	53	+ 2	44	− 5	58	+ 7	85	+ 6	47
+ 5	48	+ 7	41	+ 1	73	+ 2	*	− 2	61
− 7	61	− 5	52	+ 6	81	− 7	55	+ 3	50
+ 1	63	+ 2	49	+ 4	72	− 4	65	− 4	51
+ 8	51	− 1	55	− 1	72	− 7	95	0	67
+11	88	0	70	+ 1	72	+ 6	94	+ 3	60
+ 7	30	0	45	+ 6	64	+ 4	75	− 1	61
−18	60	0	82	− 1	75	+ 2	96	− 5	67
+ 7	50	+25	36	+ 1	72	− 1	79	− 2	65
− 1	39	+ 5	24	− 1	66	+ 8	88	− 7	67
0	37			?	*	+15	81	− 7	65
+ 1	40			*	70	+ 6	75	− 3	56
?	*			+ 2	73	+ 4	*	− 0	73
*	34			+ 1	70	−48	80	1	75
− 5	30			+ 2	83	− 3	92	+ 5	69
− 8	24			+13	63	+ 3		+12	74
0	39			+ 1	64			+ 4	72
− 3	50			− 9	70			−18	64
+ 5	57			+18	61			+ 1	67
+12	40			− 1				+ 3	71
+ 2	49							− 4	85
− 5								+ 1	

* Break in curve.

From this table we see that the knee-jerk may be large when the tension of the muscles is high, medium, or low, and that the knee-jerk may be small when the tension of the muscle is high, medium, or low. In fact one can trace no constant relation between the amount of tension of the muscles and the size of the knee-jerk. It is interesting

to see how markedly the tension of the muscles may vary without any corresponding alteration in the size of the knee-jerk. This is well seen in Charts II., III. and IV.

In the cases just studied, the tension of the muscles was determined by the position of the line of rest just after the oscillations caused by the preceding knee-jerk had ceased. Ordinarily no further change in the line of rest was seen to occur in the interval elapsing before the next blow was struck. This was found to be the case by experiments in which the records were taken on a revolving drum. Occasionally, however, such changes were seen, and in the following table two cases are reported in which considerable variation in the position of the line of rest occurred in the intervals between the succeeding knee-jerks. Since in these cases the tension of the muscles was changing almost at the moment that the blow was struck, one might expect to find here, if anywhere, that the extent of the knee-jerk was influenced by the tension of the muscles.

Description of Table IV.

The table is headed by the letters representing the names of the two men on whom the examinations were made, and by the numbers of the tables in which these results again appear in this paper. The results of the examinations are given in four columns placed beneath these letters. In the first column is recorded the position of the knee-joint just before the blow was struck; in the second, the extent of the knee-jerk; in the third, the position of the knee immediately after the oscillations had ceased; and in the last column, the change in the position of the knee, occurring in the interval before the next blow was struck.

TABLE IV.

Q [Table VIII. p. 141.]				A [Table IX. p. 142.]			
Position of line of rest just before blow was struck as compared with the original line of rest	Extent of the Knee-jerk	Change of the line of rest from position held just before blow was struck	Further change of line of rest in the interval of quiet	Position of line of rest just before blow was struck as compared with the original line of rest	Extent of the Knee-jerk	Change of the line of rest from position held just before blow was struck	Further change of line of rest in the interval of quiet
0	83	+10	−9	0	53	− 6	+1
+ 1	65	+ 4	−3	− 5	40	− 4	+1
+ 2	56	+ 2	−1	− 8	41	+ 3	+1
+ 3	55	+ 1	−2	− 4	20	− 2	+2
+ 2	42	+ 3	−2	− 4	20	− 5	+2
+ 3	59	+ 3	−2	− 7	50	+ 4	+1
+ 4	26	0	−1	− 2	60	− 3	+1
+ 3	53	+ 2	−4	− 4	30	− 2	+1
+ 1	36	+ 4	−2	− 5	17	0	+1
+ 3	39	0	−2	− 4	39	0	0
+ 1	52	+ 3	−2	− 4	49	+ 4	0
+ 2	42	− 5	−8	0	36	− 1	0
−11	70	+20	−4	− 1	44	+ 8	+1
+ 5	32	− 1	−4	+ 8	20	− 1	0
0	54	+ 3	−1	+ 7	55	+ 3	−1
+ 2	58	− 1	−2	+ 9	33	− 2	0
− 1	50	0	0	+ 7	26	− 3	+2
− 1	44	+ 3	−1	− 6	44	+11	−2
+ 1	32	+ 4	−1	+15	32	+ 8	−5
+ 4	56	+ 6	−4	+18	26	− 3	−1
+ 6	47	0		+14	36	− 3	−1
				+10	36	+ 1	−1
				+10	26	− 2	−1
				+ 7	26	− 2	0
				+ 5	33	0	0
				+ 5	24	− 1	0
				+ 4	31	+ 5	0
				+ 9	54	− 5	
				+ 4			

Even in these cases one fails to find any correspondence between the size of the knee-jerk and the changing tension of the muscles, as recorded in the third and fourth columns, or the tension of the muscles compared with the amount which they had at the beginning of the examination, as stated in the first column.

Since the tonus of the muscles is without influence upon the size of the knee-jerk, the tonus theory can hardly be taken as a satisfactory explanation of the dependence of the phenomenon upon the spinal cord. A study of these experiments reveals, moreover, that not infrequently the *flexors* as well as the *extensors* contracted in response to the blow on the ligamentum patellae. This result is a very strong argument in favor of the view that the whole process is reflex. The contraction of the flexors was shown not only by the marked changes in the position of the line of rest which occasionally occurred, but it was plainly visible in the effect which it exerted upon the extent of the oscillations of the leg following the knee-jerk.

If one refers to Table I. and Chart I. he sees that the averages of the oscillations occurring in these extremely regular observations were:—

1st extension = 100, 1st flexion = 50, 2d extension = 23, 2d flexion = 8.

In other words, he notices that the first flexion equalled about half the movement of the knee-jerk, the second extension was a little less than half the first flexion, and that the second flexion was a little more than a third of the second extension. A glance at Table V., however, shows one that this proportion is far from constant, even in the case of men who are calm and quiet at the time of the experiment. Table V. has the same form as Table I.

The averages obtained from this table are as follows, viz.:—

	1st Exten.	1st Flex.	2d Exten.	2d Flex.
G.	+ 31	— 14	+ 7	— 3
X.	+ 34	— 14	+ 8	— 4
C.	+ 94	— 47	+ 25	— 8
D.	+ 33	— 14	+ 8	— 3

These averages show a general tendency for the second extension to be larger in proportion to the first flexion, than the first flexion to the first extension or the second flexion to the second extension, a result which one would scarcely expect in case the oscillations were caused by the force of gravity and the elastic recoil of the muscles. The size of the second extension suggests that the extensors in these cases did not immediately relax.

The above experiments were upon men who were calm at the time of the examination. This was seldom the case at the first examination. The fact that a stranger was about to experiment upon them in

TABLE V.

G, curve 10					X, curve 55					C, curve 23					D, curve 39				
1st Exten. i. e. Knee-jerk +	1st Flex. −	2d Exten. +	2d Flex. −	Change of line of rest	1st Exten. i. e. Knee-jerk +	1st Flex. −	2d Exten. +	2d Flex. −	Change of line of rest	1st Exten. i. e Knee-jerk +	1st Flex. −	2d Exten. +	2d Flex. −	Change of line of rest	1st Exten. i. e. Knee-j rk +	1st Flex. −	2d Exten. +	2d Flex. −	Change of line of rest
68	31	14	6	0	29	11	7	3	0	108	42	31	1	+2	45	18	11	3	+2
21	11	6	3	0	29	?	?	?	0	117	59	33	9	0	82	22	15	3	+2
43	19	10	4	0	31	16	9	4	0	146	79	47	17	+1	68	20	13	4	+1
80	37	18	7	0	31	15	9	4	0	122	58	32	8	+2	51	21	11	5	0
65	29	13	5	0	43	19	11	4	0	125	47	26	5	0	27	12	6	3	+1
54	21	10	4	0	31	12	8	3	0	122	61	32	10	0	31	16	8	4	0
41	16	9	4	0	42	18	10	4	0	115	60	33	9	0	21	7	4	2	0
18	8	4	3	0	38	16	9	4	0	128	59	32	9	0	21	9	5	2	0
24	10	6	3	0	46	21	11	5	0	113	61	32	10	−1	32	17	9	4	0
23	10	6	3	0	26	11	7	3	0	110	57	31	?	+1	42	24	13	6	0
30	11	7	3	0	40	17	10	5	0	95	48	25	?	0	57	31	18	8	0
15	7	4	2	0	38	17	10	4	0	79	37	18	4	+1	39	19	10	4	0
19	9	5	3	0	31	12	7	?	0	82	41	19	6	0	21	9	5	2	0
15	7	4	3	0	31	12	8	4	0	93	49	25	9	−1	10	4	2	1	0
16	8	4	3	0	27	11	7	3	0	92	48	26	8	0	21	13	7	3	0
29	14	7	4	0	34	15	8	4	0	76	36	18	5	+1	19	8	5	2	0
20	9	5	3	0	33	15	9	4	0	84	43	22	?	0	24	11	6	3	0
15	6	4	2	0	39	17	10	4	0	81	41	19	6	0	17	8	4	2	0
17	10	5	3	0	34	15	9	?	0	78	39	18	?	0	20	9	5	2	0
24	12	7	4	0	27	11	7	4	0	89	48	24	?	0	37	19	10	5	0
11	5	4	2	0	45	22	12	6	0	45	15	8	?	+1	43	23	13	6	0
					33	15	8	?	0	68	34	16	?	0	31	15	8	3	0
					35	15	8	?	0	50	21	9	?	0	14	6	3	2	0
					35	15	8	4	0						24	11	7	3	0
															15	7	3	2	0
31	14	7	3		34	14	8	4		94	47	25	8		33	14	8	3	

some unknown way excited nearly all of the men, more or less. When any of them was examined a number of times, or often towards the end of the first examination when the excitement had worn off, the records were similar to those recorded in Table V. This excitement, even though slight, generally sufficed to lessen the oscillations of flexion and to exaggerate those of extension more than in the cases reported in Table V. Examples of this condition are given in Table VI.

TABLE VI.

L, Curve 15.						U, Curve 52.					
No. of Observation	Knee-jerk or 1st Exten. +	1st Flex. −	2d Exten. +	2d Flex. −	Change of line of rest	No. of Observation	Knee-jerk or 1st Exten. +	1st Flex. −	2d Exten. +	2d Flex. −	Change of line of rest
1	102	29	6	5	+ 2	1	81	5	− 2	3	− 2
2	59	31	6	2	+ 1	2	60	32	7	8	− 3
3	51	28	2	?	− 6	3	70	16	11	11	+ 1
4	68	37	7	12	− 5	4	77	11	22	1	+ 7
5	58	29	12	4	+ 1	5	85	+ 8	9	+ 1	+ 2
6	73	18	17	+ 2	+ 6	6	Foot moved spontaneously				− 7
7	81	0	46	+14	+ 4	7	55	26	12	8	− 4
8	72	19	18	4	− 1	8	65	?	?	?	− 7
9	72	18	15	4	+ 1	9	95	6	12	+ 5	+ 6
10	72	+ 2	39	?	+ 6	10	94	4	37	6	+ 4
11	64	14	21	4	− 1	11	75	9	30	3	+ 2
12	75	8	12	1	+ 1	12	96	14	4	3	− 1
13	72	8	14	3	− 1	13	79	?	?	?	+ 8
14	66	18	18	?	?	14	88	+ 5	56	+ 7	+15
15	Break in curve					15	81	21	38	+ 4	+ 6
16	70	12	16	+ 1	+ 2	16	75	13	39	0	+ 4
17	76	6	14	0	+ 1	17	Break in curve				−48
18	70	10	27	+ 1	+ 2	18	80	0	20	6	− 3
19	83	7	27	+11	+13	19	92	11	35	+ 1	+ 3
20	63	1	3	?	+ 1						
21	64	26	0	?	− 9						
22	70	+ 3	36	+14	+18						
23	61	7	9	2	− 1						

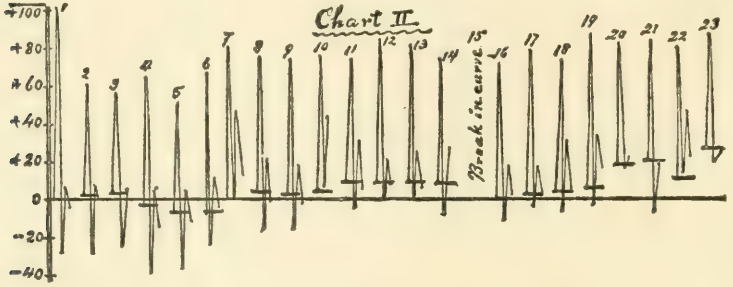
Thus in the case of L, curve 15, every observation, except number 21, from number 6 through the table, shows that the first flexion was small in proportion to the first extension, the second extension was not only large in proportion but frequently larger than the first flexion, and the second flexion was very small. In observations 10 and 22 the

first flexion did not even get back to the line of rest, and the same is true of the second flexion in observations 6, 7, 16, 17, 18, 19 and 22.

Examination of U, curve 52, shows a similar state of things. There are the same excessive oscillations of extension and small oscillations of flexion, in a large proportion of the observations, while the first oscillation of flexion does not get back to the line of rest in observations 5 and 14, and the second flexion does not get back in numbers 5, 9, 14, 15 and 19.

These peculiarities are well seen in the case of L, curve 15, recorded in Chart II.

L, Curve 15.



One cannot observe the tendency shown in these cases for the extensor muscles to check the oscillations of flexion and to increase the oscillations of extension, without noticing the remarkable exceptions to this tendency. Thus in L, curve 15, one sees the second extension to be very small in observations 1, 2, 3 and 4, and in observation 1 the second flexion is nearly as large as the preceding extension, while in observation 4 it is even larger. In U, curve 52, there is a still more interesting exception, for in observation 1 the second extension does not get back to the line of rest and the second flexion is larger than the second extension.

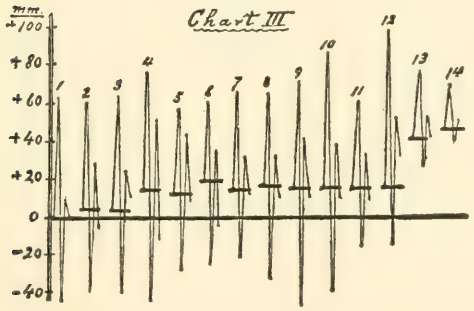
These exceptions are of the greatest interest, because they can scarcely be explained except by assuming a contraction of the flexor muscles of the knee. Such observations are of frequent occurrence and are unquestionably accurate. In certain cases, indeed, the contraction of the flexors is so strong as not only to check the second extension but to lessen the extent of the knee-jerk. C, curve 16, recorded in Table VII. and Chart III. is a case in point. The first flexion is disproportionately large in most of these experiments, and in observations 6, 8, and 9 it is as large, or even larger than the knee-jerk.

TABLE VII.

C, Curve 16.

No. of Observation	Knee-jerk or 1st Exten. +	1st Flex. −	2d Exten. +	2d Flex. −	Change of line of rest
1	63	46	9	0	+ 5
2	56	45	23	10	− 1
3	60	44	20	+ 7	+11
4	61	58	36	27	+ 2
5	44	39	31	4	+ 7
6	41	44	14	24	− 5
7	52	35	16	2	+ 2
8	49	49	18	5	− 1
9	55	62	24	5	0
10	70	56	22	5	0
11	45	30	17	6	0
12	82	31	36	+15	+25
13	36	13	11	+ 2	+ 5
14	24	6	5	?	+ 2

C, Curve 16.



The size of the second extension and the second flexion together with the shape of the curve, shows that the extensors as well as the flexors were actively contracting. In cases such as the above one sees the knee-jerk, though beginning rapidly and vigorously, to be suddenly checked and changed to flexion, which movement, as has just been shown, may be even greater than the knee-jerk. This result corresponds with the observations of certain physicians, who have told me that they have come to doubt the extent of the knee-jerk as an ac-

curate measure of the activity of the process, and that they were in the habit of basing their conclusions upon the rapidity and "jerkiness" of the phenomenon as well as upon the amount of the movement.

The fact that both flexors and extensors may be excited by the blow on the ligamentum patellae, or its results, is shown in still other cases where the oscillations of extension and flexion instead of being long and pendulum-like are short and jerky in character, so that they remind one of clonus. In these cases it is probable that both of the antagonists are actively contracting; and the leg oscillates as if swinging between two tightly stretched elastic bands. This is illustrated by the experiments recorded in Table VIII.

TABLE VIII.

Q, Curve 29[a].

No. of Observation	Knee-jerk or 1st Exten. +	1st Flex. −	2d Exten. +	2d Flex. −	Change of line of rest	Further change of line of rest
1	83	15	14	+ 7	+10	−9
2	65	12	9	+ 3	+ 4	−3
3	56	7	7	0	+ 2	−1
4	55	12	4	1	+ 1	−2
5	42	3	8	+ 2	+ 3	−2
6	59	2	11	+ 4	+ 3	−2
7	26	9	4	3	0	−1
8	53	3	6	+ 1	+ 2	−4
9	36	3	10	1	+ 4	−2
10	39	5	4	1	0	−2
11	52	4	8	1	+ 3	−2
12	42	9	1	7	− 5	−8
13	70	+29	26	+20	+20	−4
14	32	6	7	2	− 1	−4
15	54	5	7	+ 2	+ 8	−1
16	58	10	3	3	− 1	−1
17	50	2	8	0	0	0
18	44	2	7	+ 3	+ 3	−1
19	32	3	9	+ 3	+ 4	−1
20	56	8	3	+ 6	+ 6	−4
21	47	6	9	0	0	

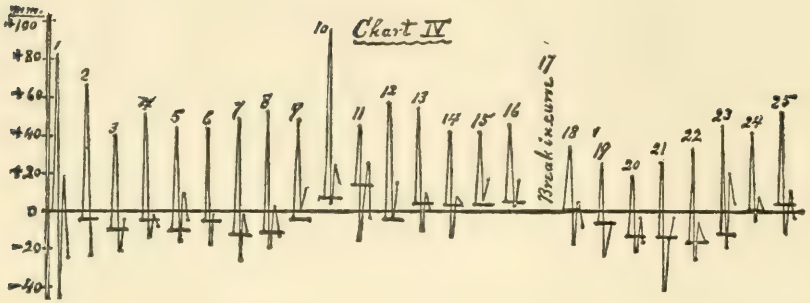
The curves recorded in this table show many irregularities, and there were other examinations made in which no prevailing tendency could be observed, but every possible variation was found. These peculiar results are explained by the fact that sometimes the flexors and sometimes the extensors of the knee exert the controlling influence. A curve 14, recorded in Table IX. and Chart IV. is a good example of the eccentricities possible to the knee-jerk.

TABLE IX.

A, Curve 14.

No. of Observation	Knee-jerk or 1st Exten. +	1st Flex. −	2d Exten. +	2d Flex. −	Change of line of rest
1	81	45	18	24	− 4
2	70	29	?	?	− 5
3	50	13	4	?	+ 5
4	56	17	2	4	− 5
5	53	6	18	+ 5	+ 5
6	48	14	2	?	− 7
7	61	14	10	+ 1	+ 1
8	63	8	13	3	+ 8
9	51	+ 4	15	?	+11
10	88	5	17	+ 7	+ 7
11	30	30	11	19	−18
12	60	0	18	?	+ 7
13	50	14	5	3	− 1
14	39	18	4	0	0
15	37	+ 1	12	?	+ 1
16	40	2	12	?	?
17	Break in curve				
18	34	17	4	7	− 5
19	30	18	0	?	− 8
20	24	8	10	3	0
21	39	29	0	10	− 3
22	50	8	10	1	+ 5
23	57	9	31	+15	+12
24	40	7	6	0	+ 2
25	49	14	7	7	− 5

A, Curve 14.



The first oscillation of flexion was prevented from returning to the line of rest in observations 9, 12 and 15. The same is true of the oscillation of second extension in 19 and 21. The first oscillation of flexion is disproportionately large in 11 and 21. The second extension is larger than the first flexion in a large proportion of the cases, yet the second flexion is larger than the second extension in 1, 4, 11, 18 and 21. The second flexion does not attain the line of rest in 5, 7, 10 and 23.

The results of these experiments can leave no doubt that under certain circumstances, at least, the flexors as well as the extensors are thrown into contraction by the blow on the ligamentum patellae or its sequellae. This discovery is of great importance not only as enabling us to understand the character of the knee-jerk, but also as a hint as to the methods of muscular coordination. It has long been thought that antagonistic muscles both act at the same time and that all the movements of the limbs are the result of finely graded differences in these opposing forces. I discovered while working in Leipzig,[1] that all the muscles of the frog's leg will respond nearly simultaneously to a strong reflex stimulus, and it seems to me that the experiments reported in this paper favor the view that the same thing is true of coordinated muscular actions in man. It is probable, however, that the contraction of the antagonist is well developed only when the action is vigorous or extended.

There can be no doubt that the blow on the ligamentum patellae resulted in a contraction of the flexor as well as of the extensor muscles in many of my experiments. How were the flexors stimulated, reflexly, or directly by the strain brought upon them by the extension of the knee?

[1] "Die räumliche und zeitliche Aufeinanderfolge reflectorisch contrahirter Muskeln." *Archiv für Anat. u. Physiol.*, Physiol. Abthl., 1885.

I am inclined to think that the extensors and flexors are both irritated by the same process. The twitch of the tendon caused by the blow on the ligament probably irritates the ends of the centripetal nerves lying in the tendon and muscle, and these nerve ends develop a stimulus which excites the reflex centres of the spinal cord. How many reflex centres are affected and how strong a reflex action is developed depends on the strength of the irritant and on the condition of the reflex mechanisms at the time. When the person is calm and quiet, only the extensors appear to be stimulated, but when he is excited, the flexors, as well, receive reflex stimuli. The extensors are irritated first and their contraction is under way before the flexors begin to contract; nevertheless, the difference in time is not great, as is shown by the fact that the contraction of the flexors often follows that of the extensors with sufficient rapidity to prevent the completion of the movement of extension. Thus one may see at the beginning of a series of experiments, when the man is excited, very small knee-jerks though the movements are sudden and violent. Gradually, as the man becomes calmer, the knee-jerks become longer and less jerky, and, finally, as he quiets down still more, they get small again. The effect of the excitement was to cause an active contraction of the flexors almost simultaneously with that of the extensors, and this antagonistic action checked the knee-jerk before completion. As the excitement became less, the flexors were stimulated less, and the contraction of the extensors was able to show itself in a larger knee-jerk. When the subject had become calm, the extensors alone were irritated, and they received a milder stimulus, so that the knee-jerk was small again. Such was the condition in the case of C, curve 3, recorded in the following Table, X.

This explanation is in harmony with what we know of reflex actions, in general. A slight irritation will call out a reflex contraction of a few muscles, and a stronger irritant applied to the same part will excite a stronger contraction of these muscles and at the same time stimulate certain other muscles. The muscles which respond to the least stimulus also contract first when more muscles are excited by the stronger irritant.

It may be asked, however, is it not possible that the contraction of the flexors is due to a direct mechanical stimulation of the muscle fibres by the sudden strain brought upon them by the rapid extension of the knee? There are several reasons why this explanation is unsatisfactory. First of all one remembers that the flexors often contract very actively when they have been subjected to a very slight

TABLE X.

C, Curve 3.

No. of Observation	Knee-jerk or 1st Exten. +	1st Flex. −	2d Exten. +	2d Flex. −	Change of line of rest
1	47	3	6	8	− 4
2	Trembling of muscles				+ 3
3	59	37	12	+ 1	+ 7
4	72	65	3	7	− 4
5	69	69	−10	13	− 2
6	76	27	17	1	+ 5
7	96	56	42	+17	+14
8	107	52	52	+ 2	+ 2
9	Trembling of muscles				+11
10	96	61	48	+13	+20
11	67	47	40	+ 7	+22
12	24				
13	Break in curve; start again				
14	82	44	11	5	+ 2
15	54	19	5	6	− 3
16	40	60	22	9	+ 2
17	27	54	− 1	24	−10
18	Foot moves spontaneously				+ 2
19	63	56	31	10	+ 4
20	40	54	29	5	+ 8
21	71	53	33	?	+ 2
22	45	25	13	1	+ 2
23	37	29	11	4	0
24	55	44	17	5	0
25	45	22	9	2	+ 1
26	54	46	20	8	− 1
27	53	33	16	3	+ 1
28	57	41	19	12	− 3

strain, and that a slight strain is unable to excite a muscular contraction. In the case of the extensors, for instance, we find that depression of the ligamentum patellae even if sudden when performed by the fingers does not cause a knee-jerk; nor does sudden flexion of the knee, when produced by the hand. The still greater suddenness of jar of a blow on the ligament is necessary to the development of the phenomenon. It is probable that the same is true of the flexors, and certainly we find that sudden extension of the knee by the hand does not cause

contraction of the flexors. The strain brought on the flexors by the extension of the knee must be a very gradual one, and not to be compared with the twitch which a blow on the ligament would produce. Moreover, the flexors often contract when the foot has made only a slight movement. Thus in observation 11, of A, curve 14, in Table IX., the foot had moved only 30 millimetres when the extension was checked by the contraction of the flexors. To have checked the knee-jerk at this point the contraction of the flexors must have started when the foot had moved even less than this distance. Such a slight movement of the foot would be accompanied by a stretching of the long flexor muscles of only at the most three or four millimetres. Nor is this an isolated example. In case of C, curve 3, Table X, observation 15 gives the movements—+ 27, — 54, — 1, — 24, that is to say, the extensors had only extended the foot 27 millimetres when a violent contraction of the flexors occurred which stopped the knee-jerk short and produced a backward swing of the foot of 54 millimetres. Many other, though perhaps less striking examples, are recorded in the table.

One can scarcely believe that such a slight strain would cause an active contraction of the flexors when he sees in the same examinations that a much greater strain has no such effect. It may be said that this argues as well against the theory of reflex as of peripheral irritation. This is not so, however, because we have evidence that the reflex centres are continually undergoing changes in irritability, while as far as we know the irritability of the muscles does not change much within short intervals of time.

I have already called attention to the fact that the flexors sometimes not only check the contraction of the extensors, but actually contracted further than the extensors had done. It is hard to understand how a muscle by contracting can irritate its antagonist to a stronger contraction than it itself made, unless indeed its antagonist was the more irritable of the two. This explanation will not suffice, because the excessive contractions of the flexors only appear as exceptions, and as a rule the contractions of the extensors are much the larger.

Summary of Results.

There are two theories of the nature of the knee-jerk; the one regards it a reflex action, the other a purely peripheral process. The reflex theory readily explains the intimate dependence of the phe-

nomenon upon the spinal cord, and the time argument, owing to our meagre knowledge of reflex times, in general, is inconclusive. The peripheral theory is not tenable, because the explanation which it offers of the dependence of the knee-jerk upon the spinal cord is unsatisfactory. It assumes that muscle-tonus is continuous, and that the irritability of the muscle to mechanical stimuli is dependent on its tension; both assumptions are without proof. Moreover, the theory is opposed by many facts.

The knee-jerk may be present when muscle-tonus appears to be wanting, and may be absent in the case of men who apparently have a normal amount of tonus. When the knee-jerk is lacking it cannot be restored by any amount of tension which can be artificially supplied to the muscle.

The tonus theory does not explain the difference which always exists in the size of the successive knee-jerks, for it is found experimentally that the size of the knee-jerk is not influenced by slight variations in the tension of the muscle; nor can the changes in the amount of the knee-jerk be attributed to alterations of the irritability of the muscle dependent on fine variations in tonus, because experiments show that the irritability of the muscle does not change within short intervals of time.

The peripheral theory does not explain the reenforcements of the knee-jerk, because reenforcing acts, unless very violent, do not alter the tension or irritability of the muscles.

The discovery of Mitchell and Lewis, that muscular contractions called out by electrical stimulation cannot be reenforced, is inexplicable by the peripheral theory though readily explained by the reflex theory.

Finally, occasionally the flexors, as well as the extensors, of the knee are seen to contract in response to the blow on the ligamentum patellae. This contraction of the flexor muscles is of reflex origin, and there is little reason to doubt that the extensors are irritated by the same reflex process. The idea that the flexors are mechanically stimulated by the strain brought on them by the sudden extension of the knee is untenable, because we know that muscles are not irritated by slight strains on their tendons, and the flexors are seen to contract when the knee has extended so little as to bring almost no strain upon them; moreover, in spite of the fact that muscle irritability does not change within short intervals of time, small knee-jerks may be seen to be accompanied by marked contractions of the flexors, and, immediately after, large knee-jerks by little or no flexor contraction.

Since only the reflex theory can satisfactorily explain the influence of the central nervous system over the extent of the knee-jerk, we must adopt it, and must look to future experimental work on reflex times to remove the apparent contradiction involved in the rapidity of the process.

[*From the Journal of Physiology. Vol. XIII. Nos.* 3 *&* 4, 1892.]

ON THE RESPIRATORY CHANGES OF THE INTRATHORACIC PRESSURE, MEASURED IN THE MEDIASTINUM POSTERIOR.

By Dr S. J. MELTZER, *New York.* (Plates VIII. A and VIII. B.).

From the Physiological Laboratory of the College of Physicians and Surgeons of the City of New York.

It is a well-known pathological fact that tuberculosis shows a decided preference for the apices of the lungs. This was often explained by the assumption that the apex is not participating fully in the respiratory movements, and that the diminished ventilation of the said locality is the cause of its predisposition for the disease. But as it is now an established teaching that an invasion of tubercle bacilli in the lungs is at the bottom of the disease, we should rather expect, that if the apex breathes less, the bacilli will have less chances of getting in there, and in consequence this part of the lungs, instead of being predisposed for the disease, should rather show a certain immunity against it. To overcome this obstacle A. Hanau[1] undertook to modify the hypothesis, by assuming that the expiration is indeed less, whereas the inspiration is rather better in the apex than in the other parts of the lungs, therefore all corpuscular elements of microscopical dimensions, like the bacilli, dust etc., have a greater chance to get in the alveoli of the apex, while their chances to get out of these by the expiration is reduced. This hypothesis would cover indeed the pathological phenomenon satisfactorily. Unfortunately for this hypothesis, the normal breathing also has to be taken in consideration. What would be the fate of the apex, if the inspiration should considerably overbalance the expiration, if more air should get into the alveoli than could come out?

Instead of speculating upon the normal status from pathological facts, we should endeavor firstly to study the normal process in due

[1] A. Hanau. *Zeitschrift für klinische Medizin.* Bd. XII.

manner by physiological methods. It is a matter pertaining to physiology to decide, if in normal breathing all parts of the lungs are equally sharing in the respiratory act. But there, in physiology, the point in question is even not raised to the rank of a problem. I failed to find in physiological literature, even a serious discussion of our question. In the face of the decided predilections, however, shown by certain parts of the lungs to certain pathological processes (Tuberculosis, Pneumoconiosis, Emphysema, etc.) physiology cannot afford to ignore this problem, or to solve it with mere theoretical speculations like the application of the physical laws of elasticity on the lungs, i.e. that an elastic band shows equal distensions in all its parts.[1]

As it is very difficult to find an exact method to ascertain directly the degree of the distensions of the apex, as compared with those of the other parts of the lungs during normal breathing, I turned my attention firstly to a phenomenon steadily accompanying those distensions; it is the change of the intrathoracic pressure coinciding with the inspiration and expiration. There are at present three different methods for determining the intrathoracic pressure. The first, and oldest method, and as it was shown by Heynsius[2], probably the most reliable one, is that which was introduced by Donders[3] and Hutchinson[4]: to connect a manometer with the trachea of a dead animal and to open both the pleuræ. We could of course not employ this method, which informs us only of the sum of negative pressure prevailing in the whole pleural cavity while the respiratory muscles are entirely at rest. Another method which seemed to be more appropriate for our purpose, is to connect a manometer carefully direct with the pleural cavity as it was practised by Fredericq[5], Bernstein[6], Weil[7] and others. For my purpose, I should have to connect two manometers at different levels of the chest wall of a living animal. I have tried it; but soon convinced myself that, just as Heynsius supposed it to be, we never get by this method the exact intrathoracic pressure as it prevails in a normal condition. By

[1] See I. Rosenthal. *Hermann's Handbuch d. Physiologie.* Bd. IV. 2 Theil, S. 180.

[2] A. Heynsius. "Ueber die grösse der negativen Drucke im Thorax beim ruhigem Athmen." *Pflüger's Archiv für Physiologie.* Bd. XXIX. 1882.

[3] *Zeitschrift für rat. Medicin.* Bd. III.

[4] Hutchinson in Todd's *Encyclopaedia of Anatomy and Physiology.*

[5] Fredericq. *Archiv de Biologie.* 1882.

[6] Bernstein, Jul. *Pflüger's Archiv.* Bd. XXVIII.

[7] Weil. *Archiv für klinische Medicin.* Bd. XXVIII.

removing carefully all the muscular tissue in one or two intercostal spaces, I could observe through intact pleura the motions of the lungs, and thus could control the state of the lungs. In this way I found out that every attempt of mine to connect the pleural cavity with a manometer was met with some degree of retraction of the lung, which if not for the direct observation, does not manifest itself otherwise.

The third method, which was introduced by Luciani[1] and I. Rosenthal[2], and which seemed to be indeed the most appropriate for my purpose, is to measure the intrathoracic pressure in the thoracic part of the œsophagus. This can be done in a living animal without further preparation, by introducing a tube (katheter) through the mouth into the œsophagus. The tube has to be of some thickness to fill out the lumen of the œsophagus, but then on one hand it interferes with the breathing, and on the other hand it makes the œsophagus contract, which of course alters the pressure within it. I therefore made an incision in the œsophagus, pushed in through the opening a small katheter, and tied the œsophagus and katheter with a rubber thread, so as to have the œsophagus air-tight around the katheter and at the same time to be still able to push the katheter up and down within the œsophagus. This was done in three rabbits. I shall briefly state that I could not discover any constant difference in the negative pressure between the upper and lower parts of the œsophagus. At the same time these few experiments were sufficient to convince me of the correctness of the statement made by Heynsius[3], that the pressure within the œsophagus does not correspond to the exact pressure of the pleural cavity, the pressure in the œsophagus being, as it was proven by Heynsius, not only considerably less, but also inconstant, and consequently unappropriate to throw light on our subject. The thickness of the œsophagus wall, the muscular tissue and its irregular contraction provoked by the presence of a foreign body (katheter) are probably the cause, as Heynsius points out, of the reduction of the pressure and its irregularity. I may add, that every act of deglutition, which occurs quite often on account of the moving of the katheter, changes the pressure within the œsophagus considerably, the change lasting for some time.

Looking out for a new method by which I could compare the intrathoracic pressure at different levels of the thorax, my attention

[1] Luciani. *Archivi per le scienze medichi.* 1878.
[2] Rosenthal, I. *du Bois Reymond's Archiv.* 1882.
[3] *loc. cit.*

was turned to the mediastinum posterior, just by the last-mentioned experiments made on the œsophagus. The only objectionable features of this locality were, as we just pointed out, the effects resulting from the thickness of the œsophagus wall and its muscular tissue. Now if we could determine the pressure alongside of the œsophagus, but outside of it, i.e. in the mediastinum posterior, there will be, we should expect, no more objections to the conclusions drawn from the results obtained in this locality as to the real state of the pressure in the pleural cavity, as the thin layer of tissue separating the mediastinum from the pleural cavity could not amount to much. The same consideration gave me at the same time an idea how to gain access to the mediastinum: alongside the œsophagus which is surrounded on its entire way by loose connective tissue; this is a convenient path, unfortunately very often preferred by the pus of retropharyngeal abscesses—why should we meet with difficulty by pushing a katheter down the same way?

It is this method and some results I obtained by it I intend to report here.

With a single exception my experiments were made on rabbits, the results therefore are so far restricted to this class of animals only. The single experiment I made on a young dog, however, convinced me that the method will be practicable in these animals also, and that the results will probably not differ materially. All the animals have been narcotized with chloral. This offers the advantage that the breathing continues regularly and is less frequent. I wish to emphasize, however, that the introduction of the katheter into the mediastinum does not alter the respiration even in the absence of narcosis. The procedure is simple, though I lost many an experiment before settling it.

The rabbit being placed on its back, the skin of the neck was cut lengthwise on the larynx, and opposite the crico-thyroideal ligament, a path was bored with a blunt instrument on the left sterno-hyoideal muscle to its outer margin, and here a narrow entrance was bored behind the lower part of the pharynx. Into this opening a katheter was introduced and pushed downward parallel and behind the œsophagus. Three centimeters, counted from the mentioned ligament, may be pushed down at once, as at this distance the blind end of the katheter is even in small rabbits still above the aperture of the chest. All further pushing has to be done carefully, groping, and in small distances, about five millimeters each. The direction should be towards the middle of the aperture, the katheter can be felt through

the skin behind the trachea, and it is advisable, while pushing the katheter with one hand, to control the lower end with two fingers just above the aperture in order to keep in the right direction, and at the same time to press the end a little backward to facilitate its entrance into the mediastinum posterior, as there is a tendency for the lower end of the katheter, while entering the thorax, to stumble against the incisura sterni, on account of the convexity of the spinal column in this region. In fact, the entrance of the katheter into the chest is the main difficulty, in older animals more so than in younger ones, not only for the reason of the greater curvature of the spinal column, but also on account of the greater firmness of the connective tissue obstructing the entrance of the chest. Drawing back the katheter should be avoided, as this might, as it would be seen later, destroy the entire experiment. Elevating the outer end of the katheter, which would facilitate its entrance into the chest, should also be avoided, as this makes the channel leading to the mediastinum too wide and facilitates the entrance of air beside the katheter. This latter should be of a very small calibre; with an English katheter No. 5 (lumen about two millimeters) I never found an insurmountable obstacle in pushing it in. The katheter is blind at the end, and has one side opening near it; I made another opening opposite the first one. The lower half of the katheter was divided by marks (small cuts) in 5 millimeters distances. The amount of pressure in the mediastinum was ascertained by connecting the katheter either with a water manometer, or with a Marey's tambour. In the latter case the respiratory undulations of the mediastinum have been recorded graphically in the usual manner, on a revolving cylinder covered with smoked paper. Below the lever writing these undulations another lever was placed marking the time in seconds. The distance between the two lines traced upon the graphic table before connecting the tambour with the mediastinum, represents the atmospheric pressure; a smaller distance means a negative, a greater distance positive pressure. The manometer, or the Marey's tambour, was connected with the katheter by means of rubber tubing, which had to be long enough to facilitate the handling of the katheter. The connection was made of course before the katheter was introduced behind the pharynx; there was no clamp or stopcock between the katheter and the manometer. Before the katheter entered into the chest, there was usually no difference in the level of the water in the two sides of the manometer, but if there was any difference, it was of course taken into account. The pushing was done, as stated, in 5

millimeters distances. At each step notes of the pressure were taken as it presented itself during the inspiration and expiration, the time of observation being from 5–6 minutes. There was hardly any necessity for taking the mean of a number of observations, as at each step hardly a difference of any account between the inspirations could be noticed. At each step, besides the pressure, the number of respirations was counted. After finishing the experiment, and killing the rabbit, I made in many experiments an autopsy to ascertain the side where the katheter found its way, and some of the localities in the mediastinum corresponding to the different distances from the crico-thyroideal ligaments as they were furnished by the preceding experiment.

Passing over to the results obtained by this method, I shall say in the beginning, that we have to distinguish between the first introduction on the one hand, and the retraction and all the following reintroductions on the other hand. While in the latter cases there were hardly any constant differences among the several parts of the mediastinum, the pressure being about the same in the entire length of it, we found in all the first introductions of the katheter, the pressure differing remarkably according to the locality of the mediastinum, which latter may therefore be divided into five sections. The first section comprises the part of the mediastinum within the first ribs and first intercostal spaces; there in most of the cases, during the inspiration, either we found no change in the pressure at all, or the change was so small that it could not be measured. In a few cases the inspiratory difference in the pressure amounted to from 2–3 millimeters of water, and only in two cases the change came up to 6 or 8 millimeters of water. Nearly the same can be stated of the condition of the pressure during the expiration—"Donders' negative pressure." In most cases there was no negative pressure, at least it was hardly perceptible, but in a few cases the negative pressure was measurable, and reached in a couple of experiments from 14 to 16 millimeters! On the other hand, there were a few other cases showing at the expiration a positive pressure of from 2 to 3 millimeters. Then a section of 2–4 centimeters length follows, where the inspiratory changes are generally larger than in the first section. In many cases a gradual increase in the amount of the inspiratory change of the pressure could be observed taking place downward, the highest amount observed being 16 millimeters; but this was by no means the rule; there have been cases where the amount of the change in a deeper place was even smaller than in a

higher one. The expiratory pressure in this section is in nearly all of the cases of a negative character, the amount being generally also larger than in the former section, but it exceeded only in exceptional cases the pressure of 10 millimeters water; a gradual increase was here the exception.

In 30% of all the cases, a section of from 1–2 centimeters length now followed, wherein again no movements at all or very small movements could be observed in the manometer during the inspirations, though sometimes the heart-beat could be recognized. The level of the water on both sides of the manometer has been, while in this section, either equal or there has been a very small difference in favour of the negative pressure; in other words, while the inspiration did not show any influence, there has been little or none at all of Donders' negative pressure.

The section which follows now comprises nearly the whole remainder of the mediastinum. In all the animals experimented upon a remarkable turn took place at this section. The inspiratory change of the pressure became considerably larger, and continued to be the same with comparatively small variations in the whole section. The exact amount of the inspiratory change varied considerably in different animals, as much as from 15 to 60 millimeters of water. There seemed to be a number of points causing the difference in the amount of the undulations, for instance, the size and age of the rabbit, the number of respirations per minute, and other points, which I do not care to enumerate, as I did not, for the present, make a close study of this question. The negative pressure in the expiratory state showed in this section in general the same sudden change in the increase, but the proportion of the increase was somewhat smaller, and there were a number of exceptions; as for instance, either without any, or with only a small increase, or again the increase having already occurred a little above this section. Below this section it occurred in some animals that the inspiratory change was again reduced to only a small amount, while there was some constant negative pressure. Usually the katheter could not be pushed, under these circumstances, much deeper. When the katheter was now retracted, step by step, it was found that in the entire mediastinum, even within the first ribs, such an inspiratory and expiratory negative pressure prevailed as was found in the 4th section, i.e. the highest attainable amount in the rabbit just experimented upon, a state which continued now to remain the same even at every new pushing down, as long as the katheter was not entirely taken out. In this latter case,

if one waited for some time before introducing it anew, there appeared to be at the reintroduction again some differences, but they were neither so pronounced, nor so constant as they appeared at the first introduction of the katheter in the mediastinum. In some of the cases in which there was a third section, i.e. a total disappearance of the inspiratory undulations before their final increase, this state seemed to remain in the same locality even at the retractions or reintroductions; when the katheter was passing this place at any time or in any direction, the inspiratory undulations used to disappear. It is worth while to mention the fact that deep inspirations, e.g. those caused by dyspnœa, were often accompanied by transient strong undulations even in the upper part of the mediastinum.

The following few tables will sufficiently illustrate the preceding descriptions.

The numbers in the first column under the heading of distance mean the distance from the crico-thyroideal ligament, the unit being 5 millimeters; thus for instance 10 means 50 millimeters from the ligament. The 2nd and 3rd columns indicate the absolute pressure in millimeters of water at each corresponding step at the inspiration or expiration, — or + indicate if the pressure was negative or positive. In the 4th column the difference of the amount of the inspiratory increase of the pressure is given. In a 5th column (when given) are the notes from the autopsy showing the corresponding place in the mediastinum; the abbreviations being:—n. m. = no motion; s. m. = small motion; v. s. m. = very small motion; n. n. p. = no negative pressure; int. = pleura intact, the lungs not collapsed.

Experiment I.

Large rabbit, 2800 gram.; katheter No. 6, pushed in at once to 10 (50 mm. distance from ligament), progressing in steps of 4 units (20 mm.). Number of respirations 36.

Distance.	Inspir.	Expir.	Diff.
10	− 18 mm.	−16 mm.	1 mm.
14	− 23 "	−19 "	4 "
18	− 71 "	−60 "	11 "
22	− 92 "	−72 "	20 "
26	−112 "	−70 "	46 "
30	−120 "	−65 "	65 "

EXPERIMENT III.

Rabbit, 1800 gram.; katheter No. 5, at once to 10, seemed to correspond to 2nd rib; respiration 46 p.m.

Distance.	Inspir.	Expir.	Diff.
10	−14 mm.	− 6 mm.	8 mm.
14	−32 "	−28 "	4 "
18	−36 "	−20 "	16 "
22	−40 "	−18 "	22 "
26	−46 "	−24 "	22 "
30	−32 "	−28 "	4 "
26	−40 "	−14 "	26 "
22	−40 "	−14 "	26 "
18	−41 "	−20 "	21 "
14	−32 "	−12 "	20 "
10	−32 "	−13 "	19 "

EXPERIMENT V.

Rabbit, 1350 gram.; katheter No. 5, pushed to 6 (30 mm.); distance between steps, 2 units (10 mm.). Respiration 36 p.m.

Distance.	Inspir.	Expir.	Diff.
6	n.m.	n.n.p.	0
8	− 4 mm.	− 2 mm.	2 mm.
10	− 4 "	− 2 "	2 "
12	− 4 "	− 2 "	2 "
14	− 4 "	− 2 "	2 "
16	−33 "	−10 "	23 "
18	−32 "	− 8 "	24 "
20	−32 "	− 8 "	24 "
22	s.m.	15 "	0 "
14	−30 "	− 9 "	21 "
10	−28 "	−10 "	18 "

EXPERIMENT VIII.

Young rabbit, 1150 gram.; katheter No. 5, pushed to 6 (30 mm.), both pleuræ intact during experiment; respiration 45 p.m.

Autopsy; katheter in the right side.

Distance.	Inspir.	Expir.	Diff.	Locality in mediastinum.
6	v.s.m.	n.n.p.	0	above aperture
8	s.m.	n.n.p.	0	1st rib
10	s.m.	n.n.p.	0	1st intercost. space
12	− 3 mm.	+2 mm.	5 mm.	
14	−18 "	−5 "	13 "	
16	−24 "	−4 "	20 "	
18	−28 "	−6 "	22 "	
20	−28 "	−6 "	22 "	

EXPERIMENT X.

Rabbit, 1700 gram.; katheter No. 6; both pleuræ visible and intact during experiment; resp. 64 p.m.

Autopsy; katheter found in left side of mediastinum posterior.

Distance.	Inspir.	Expir.	Diff.	Locality in mediastinum.
10	n.m.	n.n.p.	0	1st rib
12	−10 mm.	− 8 mm.	2 mm.	1st intercost. space
14	n.m.	− 8 "	0	2nd rib
16	− 7 mm.	− 2 "	5 mm.	3rd rib
18	s.m.	n.n.p.	0	4th rib
20	s.m.	n.n.p.	0	
	slight obstacle overcome.			
22	−35 mm.	−20 mm.	15 mm.	
24	−38 "	−23 "	15 "	
26	−38 "	−22 "	16 "	
28	−38 "	−20 "	18 "	
30	s.m.	−28 "	0 "	
28	−38 mm.	−20 "	18 "	
26	−38 "	−20 "	18 "	
24	−36 "	−23 "	13 "	
22	−38 "	−20 "	18 "	
20	−38 "	−20 "	18 "	
18	−38 "	−20 "	18 "	
16	−34 "	−15 "	19 "	
14	−35 "	−15 "	20 "	
12	−35 "	−10 "	25 "	
10	−35 "	− 9 "	26 "	
12	−35 "	−10 "	25 "	
14	−35 "	−13 "	22 "	
16	−35 "	−15 "	20 "	
18	−32 "	−12 "	20 "	
20	−38 "	−18 "	20 "	
22	−30 "	−10 "	20 "	
24	−28 "	− 8 "	20 "	
26	−28 "	− 8 "	20 "	
28	−25 "	−15 "	10 "	
30	v.s.m.	−15 "	0 "	

EXPERIMENT XIII.

Young rabbit, 1300 gram.; katheter No. 5, pleura intact, no obstacle in pushing; resp. 40, a little active.

Autopsy; katheter in left side of mediastinum posterior.

Distance.	Inspir.	Expir.	Diff.	Locality in mediastinum.
8	n.m.	n.n.p.	0 mm.	1st rib
10	– 5 mm.	0	5 "	1st intercost. space
11	– 7 "	+ 1 mm.	8 "	upper part of 2nd rib
12	– 7 "	+ 1 "	8 "	
13	– 7 "	+ 1 "	8 "	
14	– 7 "	+ 1 "	8 "	3rd rib
15	– 9 "	+ 1 "	10 "	
16	– 11 "	+ 1 "	12 "	
17	v.s.m.	0	0 "	
18	v.s.m.	0	0 "	5th intercost. space
19	– 30 mm.	– 3 "	27 "	
20	– 25 "	– 2 "	23 "	
21	– 15 "	– 3 "	12 "	
22	v.s.m.	0	0 "	
20	– 3 mm.	– 3 "	20 "	
18	– 30 "	+ 1 "	31 "	
16	v.s.m.	0	0 "	
14	– 28 "	+ 1 "	29 "	
12	– 25 "	+ 1 "	26 "	
10	– 25 "	+ 1 "	26 "	

EXPERIMENT XV.

Rabbit, 2500 gram.; pleura intact; resp. 54; katheter No. 5; no autopsy.

Distance.	Inspir.	Expir.	Diff.
10	s.m.	0	0
12	s.m.	0	0
14	– 16 mm.	– 8 mm.	8 mm.
16	– 15 "	– 3 "	12 "
18	– 16 "	– 9 "	7 "
20	– 12 "	0 "	12 "
22	– 46 "	– 19 "	27 "
24	– 49 "	– 14 "	35 "
26	– 37 "	– 10 "	27 "
28	– 37 "	– 10 "	27 "
26	– 30 "	– 4 "	26 "
24	– 30 "	– 4 "	26 "
22	– 30 "	– 3 "	27 "
20	– 30 "	– 4 "	26 "
18	– 34 "	– 4 "	30 "
16	– 34 "	– 10 "	24 "
14	– 30 "	– 10 "	20 "
12	– 35 "	– 10 "	25 "

EXPERIMENT XXV.

Rabbit, 2200 gram.; pleura intact; respir. 60, active; suspicion that the katheter is not air-tight in the mediastinum; paraffine applied to the wound a few times.

Distance.	Inspir.	Expir.	Diff.
8	s.m.	0	—
9	− 6 mm.	+3 mm.	9 mm.
10	− 3 "	+2 "	5 "
	Paraffine		
10	− 8 "	+4 "	12 "
13	− 8 "	+3 "	11 "
15	− 2 "	+1 "	3 "
	Paraffine		
15	− 2 "	+1 "	3 "
17	−40 "	+6 "	46 "
19	−40 "	+6 "	46 "
	Paraffine		
19	−42 "	+2 "	44 "

Neglecting for the present the minor points, we may say in short, that according to our experiments, the main inspiratory undulations were found to appear in the mediastinum posterior only below the 4th and 5th ribs, while above this the change of the pressure during the inspiration was either hardly measurable, or it did not amount to more than a few millimeters of water. The result being a surprise to me, I distrusted it from the beginning, the more so since in some cases a certain obstacle had to be overcome just before the larger undulations put in an appearance. (See table X. at 20 distance.)

I suspected that this sudden change might be connected in some way with a perforation of the mediastinal pleura, producing a certain degree of collapse of the corresponding lung. I therefore took the precaution to lay bare both pleuræ and to control by this means the condition of the lungs. In young rabbits this is an easy task, as it requires only to bisect the large muscles of the chest-wall; the entire lung and its movements then present themselves through the transparent pleura thoracica, in a distinct and instructive manner. Indeed, it seemed to me to be an appropriate method for the demonstration of the motion of the lungs. If there is nowhere any mention of this method, I wish to direct herewith attention to it. In older rabbits I removed carefully the intercostal muscles in the 6th and 7th intercostal spaces, so as to be able to observe the position of the

margin of the lungs. By this means I convinced myself that in no case was there the slightest retraction of the lung in connection with the sudden change in the inspiratory undulations. In fact, there was no degree of collapse in any case during the first introduction of the katheter. But after many retractions and reintroductions, the lung corresponding to the side in which the katheter was located, showed indeed in a few rabbits a tendency to collapse.

This fact demonstrates that the pleural cavity did not remain intact and that after many reintroductions air found access to it. To gain an insight as to the condition of the pleura in the other cases, I disconnected, after finishing the experiment, the katheter from the manometer, and allowed in this way the atmospheric air to enter the mediastinum directly. In the majority of the cases even then, the lung did not collapse, a sure proof that the pleura mediastinalis remained intact. In some other cases the lung did collapse, the mediastinal pleura, accordingly, had been severed indeed, but as the lung did not collapse before the disconnecting of the katheter, we may with safety conclude that in these cases no atmospheric air found access to the mediastinum beside the katheter; in other words, that at least in these cases the mediastinum remained air-tight while the katheter was introduced into it. As the revealed difference between the upper and the lower part of the mediastinum was observed (without exception) in all the cases studied, we may justly conclude that the discovered difference is neither a result of the laceration of the pleura mediastinalis, nor is it connected with the entrance of more or less atmospheric air into the mediastinum beside the katheter. With the last-mentioned point I shall deal more extensively.

The results obtained were in their extent not only unexpected, but were even in direct contradiction with my own experience in testing the intrathoracic pressure in the œsophagus.

The negative inspiratory undulations were found in this locality, at the very entrance of the mediastinum, to be of a considerably larger amount than was observed in the entire upper third of the mediastinum itself. And if we had objections against the œsophagus on account of the thickness of its wall and the effects of the muscular tissue, they were made on the supposition, that the amount of the negative pressure in the œsophagus falls short of the real pressure in the mediastinum. The natural suspicion that I myself entertained and which would certainly be entertained by others, was that the results I arrived at are only of an artificial nature, produced by the faulty method I employed, the fault being that the katheter was

not air-tight enough in the mediastinum, that probably air could get in the mediastinum alongside of the katheter, but that the entrance of the air becomes more scanty the deeper the katheter is pushed in, and thence the difference of the negative pressure between the upper and the lower parts. I paid special attention to this possible objection, and I am now going to show the untenability of it.

First of all, it should be remembered, that the present investigation was not started to ascertain the exact amount of the intrathoracic pressure, the object was merely the comparison of the amounts as they present themselves in different localities of the thorax.

Now, finding for instance, that while the inspiratory pressure in deeper parts of the mediastinum amounted to 30 millimeters water, in the upper part the pressure amounted almost to nothing or did not exceed 4 or 5 millimeters, we may admit that these are not the real amounts, that the real amounts have been reduced somewhat by the invasion of atmospheric air; but if we should go further to explain the entire difference between the upper and the lower parts only by the interference of atmospheric air, we have then to assume that the facility for the entrance of air beside the katheter is in the upper part of the mediastinum at least 6 times greater than for the entrance through it, since the amount in the upper part is at the utmost $\frac{1}{6}$ of the amount in the lower part; an assumption which is, as it seems to me, *a priori* improbable. The katheter is in the neck behind the œsophagus in close connection with the surrounding tissue, there is no natural channel leading to the mediastinum, the katheter has to bore its way thither; it is then not likely that the imaginary space around the katheter should be a better means for the communication with the outside air than the free lumen through the katheter. Then the conditions were not changed in the upper part even if a katheter with a wider lumen was employed, which could not be the case if the entire effect depended upon the rivalry between the lumen of the katheter and the space around it. To make this latter more impermeable for air in many cases before pushing the katheter down the neck and after inserting a cannula in the trachea, I have dressed the entire wound with a tightly fitting bandage surrounding the neck, and thus pressing the tissue closer to the katheter. The results have been just the same as they were found to be without this precaution. And the results remained practically the same after employing a still safer method for occluding the wound and thus excluding the atmospheric air.

By filling out the entire wound carefully with melted paraffine, any side entrance to the mediastinum is safely closed up. I tested it by artificially increasing the negative pressure to a higher amount; it remained unaltered so long as the paraffine cover remained unbroken. Although this happens indeed when the katheter is moved, the method is perfectly reliable if applied after the katheter is at rest; and this is sufficient for our purpose, since we can occlude every time anew before testing the pressure. No matter how much air entered beforehand, after safe occlusion the inspiratory change ought to be in all parts of equal amount, that is, if the invasion of the atmospheric air is at the bottom of the manifold mentioned differences. As we just stated, the difference was not affected by the occlusion (see Exp. XXV.), and consequently it cannot be simply the result of a more convenient invasion of air through a side opening in the upper part of the mediastinum.

Aside from those experimental proofs, there is a fact in the results themselves, which speaks decidedly against the supposition, that it is the access of atmospheric air by the side-ways, which cuts down the negative pressure in the upper part of the mediastinum. It is the fact that at the retraction or reintroduction of the katheter the difference disappears; there is then in the upper part the same high amount of negative pressure at each inspiration as is found to be in the lower part of the mediastinum. And we can certainly not presume that the side-ways became narrower by the retractions or reintroductions.

After all this, there can hardly be any doubt that the smallness of the amount of the negative pressure, which was found to take place in the upper part of the mediastinum during an inspiration, is not an artificial phenomenon, produced by some defect in the experiments, but shows that it is a fact indeed, that the change in the intrathoracic pressure which prevails during an inspiration, affects but little the upper part of the mediastinum!

While thus defending the entire usefulness of the method employed, so far as concerns the main object of this investigation, I am willing to admit, that unless a safe method is found by which it would be possible to exclude positively any entrance of air beside the katheter, while this is pushed into the mediastinum, the other points of the results obtained by this method are open to criticism. The amounts of the negative pressure at the inspirations as well as at the expirations, as they were obtained in the mediastinum, have no claim on absolute correctness; they may be indeed influenced by

the entrance of some air alongside of the katheter. Moreover these amounts vary with the frequency of the respiration, with the diameter of the lumen of the katheter, with the length of the tube connecting the katheter with the manometer, and perhaps with the side, on which the katheter was introduced, as the amounts from the left side seemed to be smaller than those from the right side! Concerning the negative pressure during the expiration, we should remember that in rabbits, according to Traube and I. Rosenthal, the external oblique muscles do contract in normal expirations, which would make the amount of the negative pressure in living rabbits, smaller than that given by Donders or Heynsius, who experimented on dead animals.

All these points have not received sufficient consideration in my experiments, as I was mainly interested in the comparison of the results of the different sections of the mediastinum, obtained under the same conditions. With somewhat more confidence could be regarded the result showing a constant difference in the amount of negative pressure in the different sections of the mediastinum during the expirations also. Though I shall not discuss at length this point, I wish to say that if we should even admit that air finds access to the mediastinum, and that the invaded air affects the expiratory pressure in the upper part of the mediastinum somewhat more than in the lower part, it is pretty certain that this is not the only cause of the comparatively pronounced difference in the amount of the expiratory pressure, the difference being nearly as constant and as pronounced as was the case in the inspiratory undulations!

From the very fact that there is a difference between the upper part and the rest of the mediastinum in respect to the intrathoracic pressure, it follows that, no matter what the cause of the difference may be, the mediastinum does not represent normally a connected cavity; if the cavity were so connected, there could not be any difference in its localities in respect to the prevailing pressure, since in a connected cavity the pressure is the same in all parts. It is rather to be supposed that the mediastinal walls in some way or other adhere together to such a degree, that one part can not be influenced by the pressure prevailing in another part. We can now easily understand why the mentioned difference was only present at the first introduction, and not any more at the retractions or reintroductions; because the first introduction of the katheter transforms the mediastinum into a well-connected channel, where the pressure can not be other-

wise than equal in all its parts. And as the œsophagus is naturally such a well-connected channel, we see now further why we found the same pressure in all its parts, and conceive a natural explanation for the apparently singular fact, that the respiratory changes of the pressure should be larger in the upper part of the thick-coated œsophagus, than in the upper part of the mediastinum: it is not the respiratory undulations in the upper parts of the lungs directly transmitted to the upper part of the œsophagus which we measure there, it is only the propagated pressure of its lower part transmitted there from the lower parts of the lungs.

The avowed purpose of the present investigation, was to infer the amount of the respiration in different localities from the condition of the changes in the intrathoracic pressure accompanying the respirations in the corresponding localities. Now as we found indeed that the changes of the respiration are very little marked in the upper third of the mediastinum, we should proceed to conclude that the respiration is considerably diminished not only in the apices of the lungs, but even in the entire upper third at least of the back parts of the lungs. The conclusion means in particular that the pressure in the mediastinum differs not at all or very little from the pressure in the pleural cavity, and that the pressure here may be taken as an exact expression of the degree of breathing taking place within the corresponding parts of the lungs.

The assumption that in some part of the pleural cavity there may prevail a pressure different from that present in other parts, implies further the supposition that the pleura visceralis adheres to the pleura parietalis so much as to prevent the highest pressure, prevailing in some place of the cavity, from being propagated over the whole pleural cavity. As there are no such anatomical connections between the two pleurae to establish an adherence, we shall have to look for "adhesion" in the physical sense to fill that office. Indeed it has been claimed by some authors that the "adhesion" even assists in overcoming the elasticity of the lungs. As the back part of the upper third of the lungs is just the part of the lungs which is less subject to the respiratory movements than any other part of the lungs, we may bring this point into causal connection with the assumption, that the same part takes the least share in the act of breathing, i.e., the alveoli of this part expand very little during the normal inspiration. We may assume further that the upper parts of the lungs are in the expiratory state in a less expanded condition and are better conformed to their corresponding part of the thorax

than the rest of the lungs and therefore there is none or only little negative pressure in the upper part of the thorax, while it is at rest in expiration. Indeed there would be altogether no difficulty in explaining why the upper part of the lungs should show certain exceptions, if only the fact could be sure, that the conditions I observed in the mediastinum have exactly the same bearing upon the pleural cavity and upon the lungs. But having been successful in the research, I hesitate now to draw from the discovered facts, those conclusions for which I undertook the entire investigation. It seems now to me that the facts permit also the theory, that the diminished negative pressure which was observed in the upper part of the mediastinum is restricted to its locality alone and has no bearing on the pleural cavity. The upper part of the mediastinum harbours the aorta, both venæ cavæ, the trachea, and the bronchi, all of them are connected among themselves and with the œsophagus by connective tissue. The katheter is in this vicinity separated from the pleural cavity not only by the thin mediastinal pleura, but by a pretty thick wall formed by all the tubes mentioned above, while in the lower part of the mediastinum there is indeed nothing else to separate the katheter from the pleural cavity than the thin mediastinal pleura. The appearance of the mediastinum intensifies the supposition that there exists indeed a certain anatomical difference between the upper and the lower part of the mediastinum. The slight obstacle which was often met just before reaching that portion at which the strong inspiratory undulations put in an appearance, may come from some stouter structure of the connective tissue, located at this boundary line, and which may help at the same time to prevent the propagation of the pressure from the lower to the upper part of the mediastinum. The only objection that could be made against this theory is, that according to it, that part in the upper third which is least separated from the pleural cavity should show stronger undulations; but in the region next to the apex of the lungs is contained the least amount of thoracic viscera, and just here were hardly any inspiratory undulations to be noticed. There is not such an importance, however, in this objection as to be sufficient to exclude the possibility of this hypothesis. I mean to say this:— although it seems to me that my experiments on the mediastinum make it indeed probable that the apices and the back part of the upper third of the lungs do not participate in the breathing so largely as the other parts of the lungs do, in consideration of the importance

of this conclusion, we should not consider it as proven, until it has been tested by experiments made on the pleural cavity, directly or within the lungs themselves.

Besides the relations to the breathing of the upper parts of the lungs, the condition discovered to prevail in the upper part of the mediastinum has an important bearing on the question of the origin of the respiratory undulations of the blood-pressure. Without entering into details of the very complex theme, it is sufficient to say, that with exception of a very few all the writers on this subject agree with the view set forward and developed by Ludwig, Donders and Einbrod, that the increase and the decrease of the intrathoracic negative pressure accompanying the respirations, have a great deal to do with the undulations of the blood-pressure. During the inspiration both venæ cavæ and the right auricle are, so it is generally assumed, under a considerably lower pressure than the veins outside of the thorax, which difference of pressure causes greater inrush of blood into the great thoracic veins and the right auricle, and thus more blood comes into the ventricle, etc.; the expiration on the other hand by the diminished intrathoracic negative pressure diminishes the influx of blood into the ventricle. The same conditions have, so it is calculated, an opposite but a smaller effect on the aorta. Now we have seen in our experiments that the inspiratory changes in the intrathoracic pressure are very small in the upper part of the mediastinum, amounting only to a few millimeters of water, the main change in the pressure occurring in the lower part of the mediastinum. As the upper part reaches as far deep as the 5th or 6th rib, so this part contains the entire superior vena cava, the arcus aortæ, the auricles, and a considerable part of the inferior venæ cavæ and the descending aorta. In short, the main circulatory parts which are expected to be influenced by the considerable change in the intrathoracic pressure, are located in that part of the mediastinum where, according to my experiments, very little change occurs. Thus my experiments seem to destroy nearly the entire basis, upon which the prevailing theory concerning the respiratory undulations of the blood pressure rests!

I content myself for the present with this short reference to the subject, awaiting firstly a confirmation of the facts I have stated here. I wish only to add that by the method of introducing a tube in the mediastinum posterior without influencing the respiration, it is possible to exclude entirely the respiratory undulations of the in-

trathoracic pressure, and it will thus be possible to investigate directly, the share those undulations of the intrathoracic pressure have in the undulations of the blood-pressure.

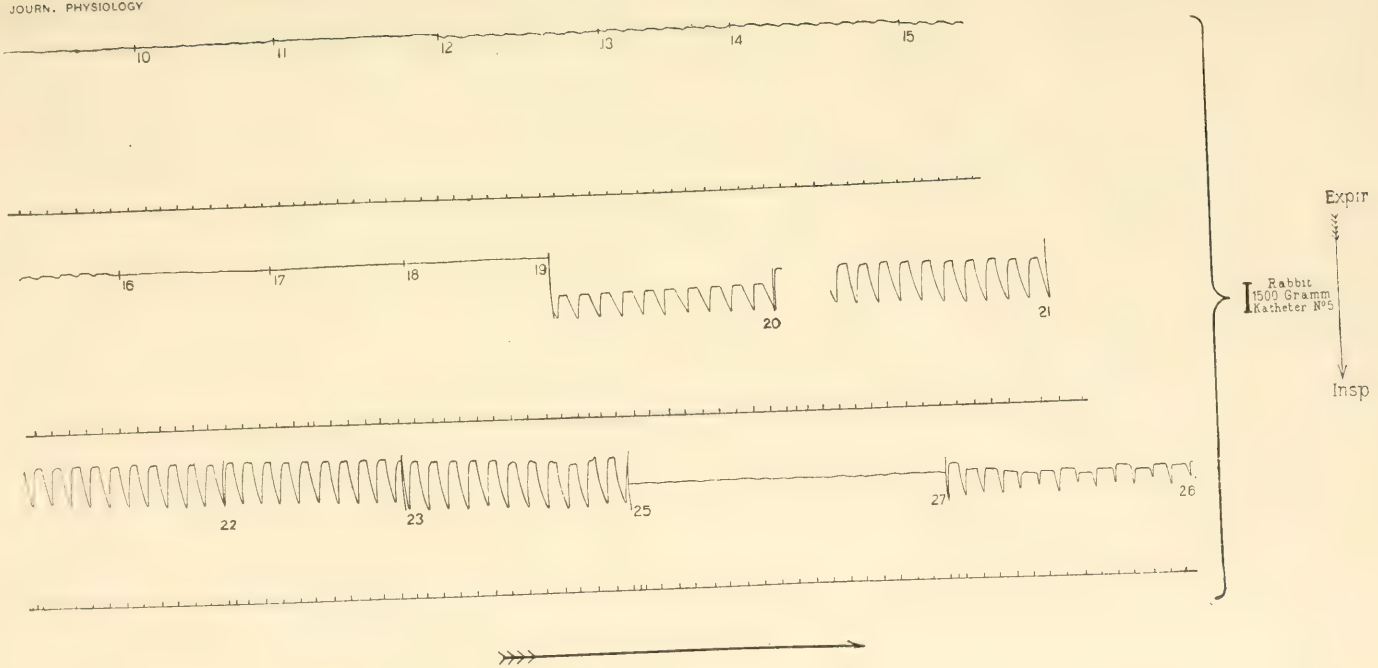
EXPLANATION OF THE CURVES.

The curves have been obtained by connecting the katheter with a Marey's tambour, the lever of which transmitted the respiratory undulations of the intrathoracic pressure on the smoked paper, which covered the revolving cylinder of a recording apparatus. The negative pressure accompanying the inspiration rarefies the air in the tambour, and thus makes the lever of the tambour descend; the ascension of the lever corresponds to the expiration. Below the inspiratory undulations the lever of a time-marker recorded the time in seconds. The distance between the lines of the two levers, traced before the katheter was introduced into the chest, represents the condition of the air in the tambour under atmospheric pressure. A smaller distance means a negative, a greater distance a positive pressure.

The Curves on Plates VIII. *A* and VIII. *B* are selected from quite a great number of curves, all of which show quite the same proportion between the undulation of the upper and lower parts of the mediastinum, the difference consisting only in the absolute dimensions of the undulations obtained from the lower parts, a difference which is even to be seen in the present two curves. Even the undulations in VIII. *B* are not nearly as large as I obtained in some animals. Each of these curves represents an entire experiment. The katheter has been pushed into the chest, in these experiments, from 6 at once to 10 units, this distance corresponding in VIII. *B* to the first ribs, and in VIII. *A* to the first intercostal spaces. The numbers on the curves mean the distances from the crico-thyroideal ligament, a unit being 5 mm. (10 means 50 mm.). After recording the undulation in one position, the cylinder was stopped and the katheter pushed one unit deeper; then the cylinder was again put in rotation, and so on until the probable end-point of the mediastinum was reached; and then the retraction followed. The position of the tambour and the time-marker remained the same during the entire experiment. The direction of the curve downward means inspiration, and upward means expiration; the marks above the undulations show the beginning, the numbers below, the end of the undulations, corresponding to the distance given in the number. In both of these experiments there has been some active expiration.

Plate VIII. *A* is obtained from a rabbit 1500 gram., with a katheter No. 5; lungs visible through pleura; *int.* means that the pleural cavity remained

intact. In the distance from 10 to 12, we see hardly perceptible undulations; from 12 to 16 they are increasing gradually; from 16 to 19 they disappear again; at 19 there is a sudden increase in the inspiratory undulation, and with only a small gradual increase remaining rather about the same to 25; at 27 there is again no motion, and at 26 they are irregular, and smaller as in the preceding section. The level of the expiratory line remained between 10 and 12 like it was before the introduction of the katheter, from 12 to 19 there was a very slight degree of negative pressure; its main increase occurs suddenly at 19 and continues to be about the same in the remainder of the mediastinum, being even a little more pronounced in the last section (27), where no more inspiratory undulations are to be seen. Plate VIII. *B* is obtained from a rabbit of 1800 gram., with a katheter No. 5, the pleural cavity remaining intact even after admitting air to the mediastinum. We meet in this curve in the main with the same conditions as in VIII. *A*, with the difference that the large undulations appear in a deeper part of the mediastinum; there is a visible increase in the inspiratory undulations at the retraction, and there is no negative pressure at the expiration, rather a little positive pressure throughout the experiment, the contraction of the expiratory muscles being pronounced.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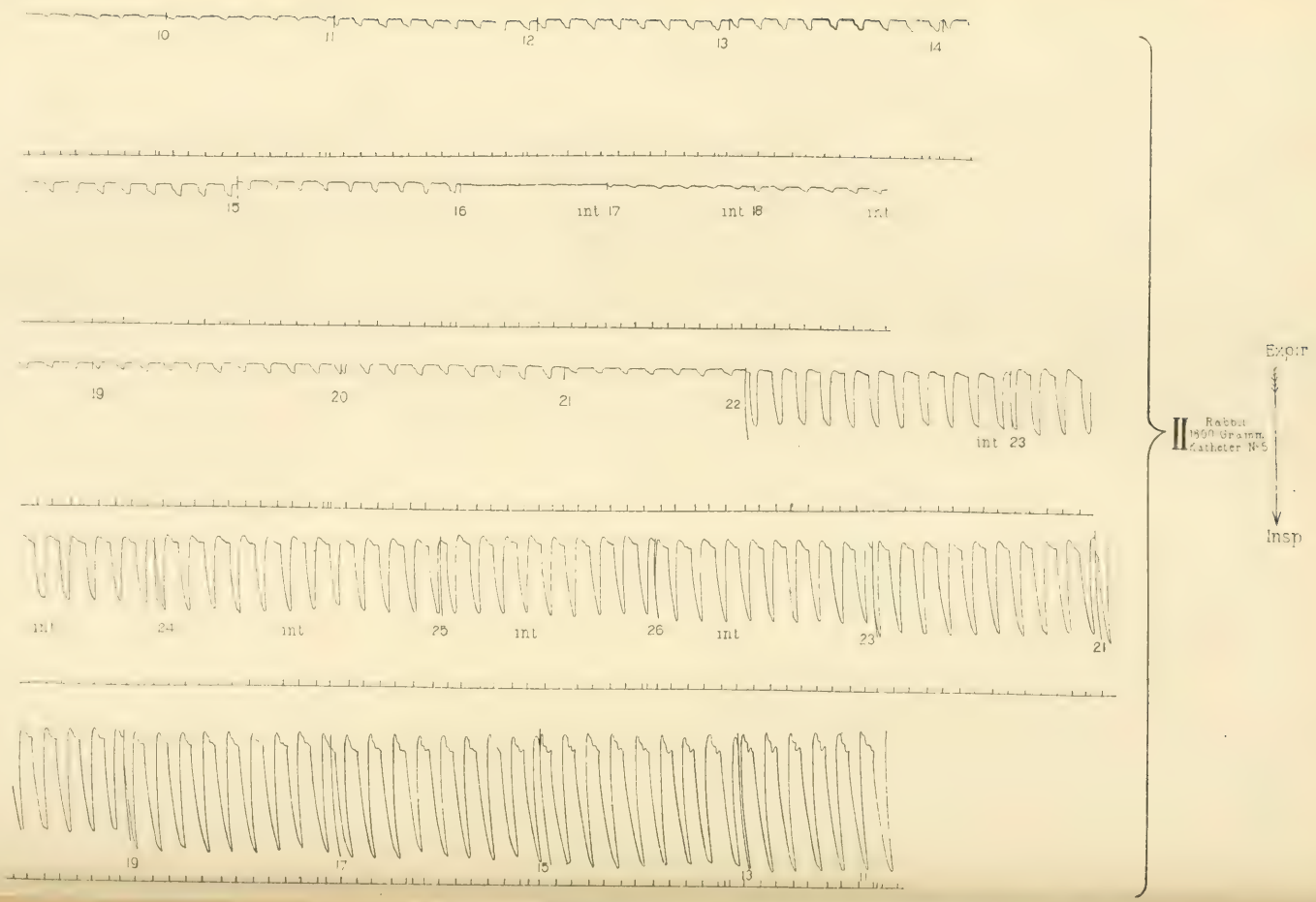
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Separatabdruck aus dem "Centralblatt für Physiologie" vom 19. November 1892, Heft 17.

Ueber den Gleichgewichtssinn.

Von **Frederic S. Lee**, Ph.D.,

Demonstrator of Physiology in the College of Physicians and Surgeons (Medical Department of Columbia College), New York.

Die Frage über die Bedeutung des Ohres für die Haltung und Bewegung des Körpers bei Wirbelthieren ist noch eine offene. Die theoretischen Ueberlegungen von Goltz, Mach, Breuer und Crum Brown haben keine allseitige experimentelle Bestätigung gefunden und manche neuere Autoren leugneten jeden Zusammenhang zwischen dem Ohre und der in Rede stehenden Function.

Während des letzten Sommers habe ich im Marine Biological Laboratory in Woods Holl, Mass., eine Reihe hierhergehöriger Experimente an einer Species von Haifischen (Dogfisch, Galeus canis) ausgeführt. Sewall, Steiner und Loeb haben bereits früher an derselben Thiergruppe gearbeitet und sind hierbei zu verschiedenartigen Schlüssen gekommen. Ich habe nach zweierlei Methoden gearbeitet; erstens habe ich die Ampullen der Bogengänge und das Vestibulum gereizt — die Reizung war eine mechanische, hervorgebracht durch Druck mit einer stumpfen Nadel oder mit einem Stückchen Watte — und zweitens, die verschiedenen in Betracht kommenden Akusticusäste durchschnitten. Ich theile hier die Hauptresultate kurz mit und behalte mir vor, die Einzelheiten meiner Experimente, sowie eine volle Erörterung derselben in einer ausführlichen, demnächst zu erscheinenden Arbeit zu veröffentlichen.

Kurz zusammengefasst, darf ich sagen, dass meine Experimente auf die innigste Beziehung zwischen Ohr und Erhaltung des Körpergleichgewichtes hinweisen, und zwar sowohl im Ruhezustand als während der Bewegung.

Der genannte Fisch zeigt wohlcharakterisirte, compensirende Bewegungen der Augen und Flossen, wenn er um seine verschiedenen Axen gedreht wird, welche Bewegungen ich sowohl am normalen, als am operirten Thiere sorgfältig studirt habe. Wenn der Körper des normalen Thieres erst horizontal gehalten und dann um seine Längsaxe, d. h. in einer transversal verticalen Ebene, gedreht wird, so drehen sich dessen Augen um dieselbe Axe, jedoch in entgegengesetzter Richtung, während die Flossen sich um dieselbe Axe und in derselben Richtung bewegen. So z. B. verursacht das Rollen des Körpers nach links eine Drehung des linken Auges aufwärts und des rechten abwärts, das linke Flossenpaar wird stark nach abwärts, das rechte stark nach aufwärts, die beiden Rückenflossen werden stark nach links und die Bauchflosse wird stark nach rechts gebogen. Wenn der Körper horizontal gehalten und darauf um seine verticale Axe, d. h. in einer horizontalen Ebene gedreht wird, so bewegen sich die Augen um dieselbe Axe, aber in entgegengesetzter Richtung,

die paarigen Flossen bewegen sich gar nicht, während die Rückenflossen sich nach der entgegengesetzten Seite und die Bauchflosse nach derselben Seite bewegen. Beispiel: die Rotation des Körpers um seine verticale Axe nach links verursacht eine Drehung des linken Auges gerade vorwärts und des rechten nach hinten innerhalb der Augenhöhle, die Rückenflossen wenden sich dabei rechterseits und die Bauchflosse geht nach links. Wenn schliesslich der Körper horizontal gehalten und um seine transversale Axe, d. h. in sagittaler Ebene, gedreht wird, so rotiren die Augen in umgekehrter Richtung und stehen schräg, die medianen Flossen behalten ihre frühere Stellung und die paarigen Flossen bewegen sich in der Richtung des Körpers, jedoch umgekehrt zur Bewegungsrichtung des Kopfes. So z. B. bewirkt das Untertauchen des Fisches mit dem Kopfe nach unten und dem Schwanze nach oben eine Drehung des vorderen Augenpoles nach oben und des hinteren nach unten, die medianen Flossen bleiben unbeweglich und die paarigen Flossen wenden sich nach oben.

Nach der Theorie, dass die halbzirkelförmigen Canäle diejenigen Organe darstellen, vermittelst deren das Thier den Wechsel seiner Lage aus einer Ebene in eine andere im Raume beurtheilt, würde man erwarten, dass eine Reizung der verschiedenen Ampullen durch entsprechende compensirende Bewegungen beantwortet werden müsste; und dies ist auch in der That der Fall. Reizung der Ampulle des vorderen verticalen Canals bewirkt eine Drehung des Auges derselben Seite nach oben, wobei jedoch der vordere Pol mehr gedreht wird als der hintere, weshalb das Auge eine Schrägstellung annimmt. Das Auge der anderen Seite dreht sich nach abwärts — der hintere Pol mehr als der vordere — daher wiederum eine Schrägstellung. Die paarigen Flossen der gereizten Seite bewegen sich nach abwärts, die der entgegengesetzten Seite nach aufwärts, die Rückenflossen beugen sich der gereizten Seite zu, die Bauchflosse wendet sich nach der entgegengesetzten Seite. Man vergleiche diese Lageveränderungen mit den normalen compensirenden Bewegungen, welche bei der Drehung des Körpers um seine longitudinale und transversale Axe entstehen. Reizung der Ampulle des hinteren verticalen Canals veranlasst gleichfalls das Auge derselben Seite, sich nach aufwärts zu drehen, den hinteren Pol jedoch mehr als den vorderen, während das andere Auge nach abwärts geht, der vordere Pol mehr als der hintere. Die Flossen bewegen sich in derselben Richtung wie bei Reizung der vorderen verticalen Ampulle. Reizung der Ampulle des horizontalen Canals verursacht eine Vorwärtsdrehung des gleichseitigen und eine Drehung nach hinten des anderen Auges: die Rückenflossen bewegen sich nach der zur gereizten entgegengesetzten Seite, die paarigen Flossen bleiben gewöhnlich unbewegt.

Von grösstem Interesse in dieser Beziehung sind die Folgen der Durchschneidung der zu den verschiedenen Ampullen gehenden Nerven. Wird der zur vorderen verticalen Ampulle gehende Nerv allein, oder der zur hinteren verticalen Ampulle gehende Nerv allein durchtrennt, so beseitigt dies keine der normalen compensirenden Bewegungen, die bei Drehung in einer der drei Ebenen entstehen. In der sagittalen Bewegung jedoch, obschon dieselbe normal compensirt ist, bewegt sich das Auge der operirten Seite in gleicher Richtung

mit dem Kopfe und das andere Auge in entgegengesetzter Richtung, wenn nur die vordere verticale Ampulle allein ausgeschaltet wird, während genau das Gegentheil passirt, wenn der zur hinteren verticalen Ampulle gehende Nerv allein durchtrennt wird. Gleichseitige Durchtrennung des zur vorderen verticalen Ampulle der einen und zur hinteren verticalen Ampulle der anderen Seite gehenden Nerven ergibt denselben Erfolg, als wenn einer der gedachten Nerven allein durchtrennt worden wäre; nur ist der Effect intensiver. Durchtrennung der Nerven der vorderen verticalen und hinteren verticalen Ampulle derselben Seite scheint die Vollführung der normalen Compensation nicht zu beeinflussen; nur nehmen Augen und Flossen permanent eine falsche Position ein, und zwar eine solche, wie sie Augen und Flossen annehmen, wenn man das Thier um seine Längsaxe von der operirten Seite wegdreht. Solch ein Fisch hat die Tendenz, sich auf die operirte Seite zu neigen und schwimmt entweder mit der betreffenden Seite nach abwärts gerichtet, oder er rollt sich um die Längsaxe. — Durchtrennung der Nerven, welche zu den beiden vorderen verticalen Ampullen gehen, verursacht eine permanente Schrägstellung der Augen, die vorderen Pole nach abwärts und die hinteren nach aufwärts gerichtet. Die Compensation scheint normal zu sein, ausgenommen, wenn das Thier mit dem Kopfe nach abwärts um die Queraxe gedreht wird; dann scheint die Compensation oft zu fehlen. Ein solches Thier hat die Neigung, mit dem Kopfe nach abwärts, gegen den Boden seines Aquariums hin, unterzutauchen. Genau das Entgegengesetzte in jeder Beziehung zeigt ein Fisch, dessen beide, die hinteren verticalen Ampullen versorgenden Nerven durchtrennt sind. Hier sind die Augen auch schräg gestellt, doch ist die vordere Fläche nach oben und die hintere nach unten gerichtet. Die Compensation ist wahrscheinlich normal, ausgenommen wenn der Körper mit nach oben gerichtetem Kopfe um seine Queraxe gedreht wird: das Thier bleibt mehr oder weniger aufrecht im Wasser, oft mit der Nase in der Luft schwimmend. Man vergleiche die Resultate in diesen beiden letzten Fällen mit den compensirenden Bewegungen eines normalen Fisches, den man um seine Queraxe dreht. — Durchtrennung sämmtlicher Nerven, die zu den vier verticalen Canälen gehen, beseitigt alle compensirenden Bewegungen in beiden verticalen Ebenen; sie bleiben intact für die horizontale Ebene, d. h. bei Rotirung des Körpers um seine verticale Achse, so lange die beiden horizontalen Ampullen functioniren. — Durchtrennung eines Nerven, der zu einer der horizontalen Ampullen geht, erzwingt weder nothwendigerweise eine abnormale Position der Augen und Flossen, noch beseitigt sie die Fähigkeit des Thieres, in horizontaler Ebene zu compensiren. Diese Fähigkeit wird jedoch ganz vernichtet, sobald auch der andere horizontale Nerv durchtrennt wird: dann konnte man das Thier die schönsten Circus-Bewegungen, sowohl nach rechts als nach links, ausführen sehen. — Nach Durchtrennung der Nerven, die zu sämmtlichen Ampullen der einen Seite gehen, ist Compensation noch möglich: beim Schwimmen macht das Thier ausgezeichnete Rollbewegungen um seine Längsaxe nach der operirten Seite hin. In Ruhe ist der Körper ein wenig nach der operirten Seite gekrümmt, die auch abwärts geneigt ist. Augen und Flossen nehmen die Stellung

ein, wie nach Ausschaltung der vorderen und hinteren verticalen Ampulle derselben Seite. Durchtrennung der Nerven sämmtlicher Ampullen auf beiden Seiten beraubt das Thier jedweder Fähigkeit, in irgend einer Ebene zu compensiren. Dies ist schlagend. Dabei schwimmt der Fisch ganz unregelmässig, bald auf der Seite, bald mit dem Bauche nach unten, bald nach oben.

Experimente am otolithischen Theile des Ohres, d. h. Sacculus, Utriculus und Lagena, ergaben nicht so ganz klare Resultate, wie die vorher beschriebenen. Es zeigte sich, dass es möglich war, durch Reizung verschiedener Abschnitte der otolithentragenden Nervenendigungen alle Augenbewegungen zu bewirken, welche durch Reizung der verschiedenen Ampullen derselben Seite erzielt worden sind; es war aber nicht möglich, die Auslösungsstellen in bestimmten Theilen des Vestibulum genau zu localisiren. Der Versuch, den vestibulären Theil des Akusticus zu durchschneiden, ohne die zu den Ampullen gehenden Aeste zu verletzen, erwies sich als unausführbar. Es ist daher der Versuch gemacht worden, eine Functionsausschaltung der vorher erwähnten Theile durch Entfernung der Otolithen zu erzielen, und somit gleichzeitig die statischen, respective geotropischen Functionen der Otolithen selbst zu studiren. Die Entfernung der Otolithen aus einem Ohre beeinflusst in keiner Weise die compensirenden Bewegungen in den verschiedenen Körperebenen. Das Auge auf derselben Seite ist dauernd heruntergedreht, das andere Auge ist gehoben, die Flossen sind flectirt im entgegengesetzten Sinne. Forcirte Bewegungen sind in der Regel abwesend. In den Ausnahmefällen, wo sie vorkommen (Rollen um die Längsaxe nach der operirten Seite hin), war es sehr fraglich, ob nicht auch die Function der halbkreisförmigen Canäle durch den Eingriff ausgeschaltet worden war. Entfernung der Otolithen in beiden Ohren zerstört nicht nothwendigerweise die compensirende Fähigkeit des Fisches. Seine Bewegungen lassen entschieden einen „Mangel an Ballast" erkennen, und der Fisch ruht zeitweise auf dem Rücken oder auf der einen Seite, anstatt wie gewöhnlich auf dem Bauche zu liegen.

Durchtrennung des ganzen Akusticus auf der einen Seite verursacht Effecte, auf die man schon aus den vorhergehenden Experimenten schliessen konnte: im Ruhezustand permanente falsche Stellung der Augen und Flossen, Krümmung des Körpers nach der operirten Seite und die Tendenz, sich mehr oder weniger nach dieser Seite abwärts zu neigen. Während der Bewegung kann man minutenlang wunderschöne Rollbewegungen nach der operirten Seite hin beobachten, obschon auch normales Schwimmen möglich ist. Auch compensirende Bewegungen von Augen und Flossen sind noch möglich. — Durchschneidung beider Gehörsnerven zerstört endlich vollständig die Fähigkeit des Thieres, sich in gewöhnlicher Weise zu halten und zu bewegen. Es scheint oft für den Fisch gleichgiltig zu sein, ob er auf dem Bauche, auf dem Rücken oder auf der Seite liegt. Seine Bewegungen sind ganz unregelmässig: er schwimmt auf dem Bauche, oder Rücken, oder auf der Seite; er schlägt Purzelbäume, macht Roll- und Circus-Bewegungen. Die Augen und Flossen sind in normaler Lage und können willkürlich bewegt werden, aber alle compensirenden Bewegungen sind verschwunden.

Reprinted from *The Journal of Physiology*, Vol. XV, No. 4, 1893.

A STUDY OF THE SENSE OF EQUILIBRIUM IN FISHES. I.

By FREDERIC S. LEE, Ph.D., *Columbia College, New York.*

Contents.

I. Introductory and Historical.
II. Anatomy and Methods.
III. Compensating Movements.
IV. The Acoustic Nerve.
V. The Semicircular Canals.
1. The anterior canals.
2. The posterior canals.
3. The anterior and posterior canals combined.
4. The external canals.
5. All canals combined.
VI. The Vestibule.
VII. Summary of Results.
VIII. Bibliography.

I. Introductory and Historical.

A complete theory of the so-called "equilibrium" function of the internal ear ought to be competent to explain three classes of facts, viz. the equilibrium phenomena of the resting body, those of the body moving in a straight line, and those of the body moving in a curve. The first comprise statical, the last two dynamical, phenomena. In harmony with this classification are the terms statical and dynamical functions of the internal ear or of the acoustic nerve. It would perhaps not be going beyond the bounds of physical nomenclature, and it would certainly be helpful, to introduce into physiology the terms statical and dynamical equilibrium, the resting body being normally in the former state, the body, when moving normally, being in the latter. The movement of a body in a straight line has been called translatory, or progressive; that of a body in a curve about an axis, rotational. Among the multitude of physiologists who have investigated the functions in question, a few have recognized clearly the above principles. The failure on the part of many to comprehend them has unfortunately introduced confusion into the subject. The mechanism of equilibrium

has been studied experimentally in a variety of Invertebrates and Vertebrates, most carefully in the latter. For the present confining our attention to this group, it is generally agreed that the impulses coming to the brain, from the eyes, the muscles and the skin are valuable in enabling the central organs to co-ordinate the work of the body muscles and thereby maintain equilibrium. But the weight of evidence localizes the chief end-organs of the "equilibrium" sense in the ampullæ of the semicircular canals and the otolith-bearing parts of the auditory vestibule. Of all Vertebrates, Birds and Fishes would *a priori* be expected to yield the best results in a study of equilibrium phenomena, since their lives are spent so largely in a fluid medium, out of contact with a solid supporting body. As a matter of fact, Birds naturally have been most studied and have afforded the strongest evidence. Amphibians and Mammals have tended to confirm this. But thus far Fishes have appeared to offer exceptions to, and in the minds of some greatly to weaken, or even nullify, the testimony elsewhere obtained. The present investigation was carried out, quite independent of previous work, from a desire to discover the equilibrium mechanism in this group of animals and was unprejudiced by any previous detailed knowledge of the nature of the problem. In going over the literature, since it was completed, the writer has been gratified to learn how closely it harmonizes with the work of others upon other groups. The experiments here recounted were performed, with a very few exceptions, upon good-sized specimens of *Galeus canis* (Mitchill), the common smooth dog-fish, or dog-shark, of the Atlantic coast. The few exceptions were five specimens of the skate, *Raja erinacea* (Mitchill). The work was performed during the months of August and September, 1892, at the Marine Biological Laboratory, Woods Holl, Mass. It is a pleasure to acknowledge my great indebtedness to Dr. Jacques Loeb for valuable advice and suggestions. A brief statement of the results of other workers may be of interest and value.

After Flourens, the most important pioneer work in this field was done by Goltz, Mach, and Breuer. The labours of these investigators are so well known, that it will suffice to state their views in brief. Flourens (1824, et seq.)[1] cut the canals in pigeons and other birds and in rabbits. As to function, his own words are, "Il y a donc dans les canaux semi-circulaires . . . une force qui contient et modère les mouvements. . . . Le canal antérieur modère les mouvements d'arrière en avant; le canal postérieur, les mouvements d'avant en arrière; le canal horizontal, les mouvements de gauche à droite et de droite à gauche."

[1] A bibliographical list will be found at the end of this article.

Goltz (1870) removed portions of the canals of pigeons and concluded, that they constitute "eine Vorrichtung, welche der Erhaltung des Gleichgewichts dient. Sie sind so zu sagen Sinnesorgane für das Gleichgewicht des Kopfes und mittelbar des ganzen Körpers."

Mach (1873–5) made a great variety of careful experiments upon the rotation of men, pigeons and rabbits, and came to the belief, that "Die Annahme, dass ein Theil des Labyrinthes Organ der Bewegungsempfindung sei, namentlich dass die sechs Ampullen der Bogengänge den sechs paarweise entgegengesetzten Grundempfindungen der Drehung entsprechen, erklärt alle hier beschriebenen und auch die Flourens'schen Versuche bis in Detail."

Breuer (1873–90) has done the best and most complete experimental work upon the parts of the ear in the living animal, chiefly in pigeons. He has carefully reviewed the results of others, has carried the analysis of the subject farther and has drawn wider conclusions than any other investigator. He believes "dass die Bogengänge selbst nur die Perception von Rotationsbewegungen, Winkelbeschleunigungen, besorgen können." This leaves the sensations of progressive movements and those that lead to the perception of the position of the body in space to be accounted for. These he believes to be mediated by the otolith-bearing nerve endings, the *maculæ acusticæ*. "Wenn wir annehmen, dass die Gravitation der Otolithenplatten, ihr Zug an den Zellhaaren, die Nervenendstellen errege und dieser Reiz im Centrum die Vorstellung von der Lage des Kopfes hervorrufe, so erscheint der Säckchenapparat des Labyrinths als ein völlig geeignetes Sinnesorgan zur Perception unserer Lage im Raum. Zu dieser Annahme erscheinen wir durch die eben berührten Thatsachen berechtigt und genöthigt. Veränderungen in den Empfindungen der Otolithenmembranen, welche nicht von Rotationsempfindungen begleitet sind, rufen im Centrum die Vorstellung progressiver Bewegung hervor."

At about the same time, Crum Brown (1874), studying the phenomena of rotation in man, came independently to the conclusion that man possesses a special sense of rotation, the peripheral organ of which is constituted by the six semicircular canals.

Excepting Flourens, the conclusions of these pioneers, while differing in details, harmonize in assigning definite functions of the same general nature to the semicircular canals. Whether they are sense-organs for body equilibrium, or for movement, or for rotation, is for the present immaterial. Goltz, Mach, Breuer, and Brown agree in regarding them as sense-organs existing at the peripheral end of afferent nerves; at the distal end of the efferent nerves, connected in

the central nervous system with this afferent system, are the skeletal muscles. A reflex arc is thus constituted. The impulses travelling along the ampullar branches of the acoustic nerve give rise to definite, orderly, apparently purposeful reflex actions. It is unnecessary to go into the details of the controversy, to which the above work has given rise. Most physiologists are inclined to accept the essential truth of the views stated. As I have said, Fishes have seemed to afford testimony against it. Tomascewicz, Cyon, Kiesselbach, Sewall, Steiner, and Loeb have studied the phenomena in these animals. Tomascewicz (1877), who holds to the fantastic idea that the canals mediate the perception of the direction of sounds, could obtain no motor reactions upon rotating fishes (presumably Teleosts). She destroyed the labyrinth in six individuals, whether on one or on both sides is not stated. Of the two which survived the operation, one lived a few hours, the other three days; both swam normally. The author does not regard this part of her work as important, and barely mentions it in an appendix to a paper that is devoted to a consideration of the question in higher vertebrates.

Cyon (1878) destroyed the membranous labyrinth on one and on both sides in a few specimens of Cyclostomata (Petromyzon) and always obtained forced movements.

Kiesselbach (1882) cut without result the horizontal canals on one side and on both sides in carps.

Sewall (1884) was the pioneer in the work upon the Elasmobranchs. He cut the canals in sharks and rays without effect, stimulated and destroyed the ampullæ, lacerated the vestibule and removed the otoliths. He made a number of interesting and valuable observations of forced and abnormal movements, and even noticed some of the eye movements following stimulation of the ampullæ. But, unfortunately working under disadvantages, he studied only the immediate effects of the operation (one to six hours) and hence could not appreciate the significance and mutual relationships of his results. Their inconstancy and the impossibility of connecting a particular result with a definite portion of the labyrinth prevented him from deducing a general law and forced him to the statement: "The positive disturbances of equilibrium so often witnessed, the reflex nystagmus following mechanical stimulation of the ampullary nerves and the vestibular sacs, and the vomiting sometimes succeeding injury of the labyrinth, all point decidedly toward some sort of functional relation between the ear and the sense of equilibrium. But as it appears that the most extensive lesions of the labyrinth and its nerves may be completely devoid of any

effects upon the equilibrium of the fish, it would be a bold assumption to consider that apparatus a special sense-organ, in the usual acceptation of the term, for the preservation of the equilibrium of the body."

Steiner (1886–8) worked upon similar forms (Scyllium). He found it possible to cut and remove all six canals without causing any disturbance of movement. Removal of the otoliths on one side, or attempts at removal, with pincers, with or without section of the canals, invariably caused disturbances, usually rolling movements to the operated side. But removing the entire contents of the labyrinth cavity and filling it with paraffin never affected locomotion! The experiments are reported briefly and it is impossible to judge of the method or of the care with which they were performed. No statement is made of the general condition of the animals after operating, nor of the length of time during which they were observed. "Winking" of the eyes was noticed at times during the operations. This was not given special study, but ultimately led the author by a jump to the conclusion "dass die halbzirkelförmigen Canäle der Haifische so wenig wie der *N. acusticus* zu den Bewegungen resp. deren Gleichgewicht in irgend welcher unmittelbaren Beziehung stehen und dass die Störungen, welche man nach mechanischem Angriff auf den Vorhof thatsächlich beobachtet, Zwangsbewegungen sind, welche ihre Ursache in einer mittelbaren Läsion des Nackenmarkes an der centralen Ursprungsstelle des Hörnerven haben."

Of all the investigators of the Fishes, Loeb (1891) has done the most valuable and the most suggestive work. He has observed carefully and described in detail the phenomena resulting from severance of one or both acoustic nerves in Scyllium. He has also removed the otoliths from the labyrinths and interpreted the effects in general accordance with Breuer's theory of their statical function. The otolithic organs are "geotropic" organs, serving for the orientation of the animal body in relation to the earth. My own results in the matters treated by him are in harmony with his.

As is readily seen from the above references, the question at hand has been studied very incompletely in the Fishes. The hackneyed and uncertain experiment of cutting the canals has yielded, as might have been foretold, both positive and negative results. Most of the experimenters have sought after gross locomotor disturbances simply, forced movements; if these fail, the theory is refuted. I trust that the following account will show that the matter is not so easily settled, that, on the contrary, careful experimentation and careful observation of details are necessary, that the observed facts can have but one

interpretation, and that the Fishes bring the strongest testimony to the correctness of the theory that localizes in the ear the sense-organs of body movement and body equilibrium.

II. Anatomy and Methods.

In the following account, the anatomical nomenclature of Retzius is employed, since it is doubtless destined to prevail in Comparative Morphology. The terms need no special explanation. Attention is, however, called to the fact that Retzius distinguishes the canals and their ampullæ as anterior, posterior and external, instead of anterior vertical, posterior vertical, and horizontal. The anatomy of the ear of *Galeus canis* has not been exhaustively described. It does not appear to differ fundamentally from that of other Elasmobranch forms of the same Order, and resembles especially that of *Acanthias vulgaris* (Risso), as described by Retzius. The perilymphatic cavity is large, irregular, surrounded by cartilaginous walls, and is by no means filled by the membranous ear. The latter is anchored in its place by a complicated network of connective tissue. In the membranous labyrinth an elongated *utriculus* bears at its anterior end, below, a large ovoid *recessus utriculi*, containing a *macula acustica* with an otolith. This otolith is flattened and its plane lies in general horizontal, descending some 4° to 6° in extending laterally. Dorsal to the *recessus* the utricle receives the anterior openings of the anterior and external semicircular canals; at its posterior end it is prolonged dorsally into the large *sinus superior*, into which open the posterior ends of the two mentioned canals. Below, the utricle opens freely by an elongated slit into the *sacculus*. The line of demarcation between these two main divisions of the vestibule is not indicated superficially. The *sacculus* is larger than and lies posterior to and below the *utriculus*. At its ventro-posterior portion is the small recess, the *lagena*, the representative of the *cochlea* of higher forms. On its postero-median aspect the *sacculus* receives the *ductus canalis posterioris*, which places it in communication with the posterior canal. It contains a large *macula acustica*, bearing a large otolith, which extends over into the *lagena*. This saccular otolith is flattened laterally and differs from that of the utricle in extending approximately vertical. Its plane is a somewhat undulating one but may be said to incline laterally from the vertical 20° to 25° in descending. The lagenar otolith is a knob-like extension of that of the saccule. The anterior (vertical) and the external (horizontal) semicircular canals at their anterior ends enter the utricle side by side just beyond their ampullæ; posteriorly and above, they open into the wide

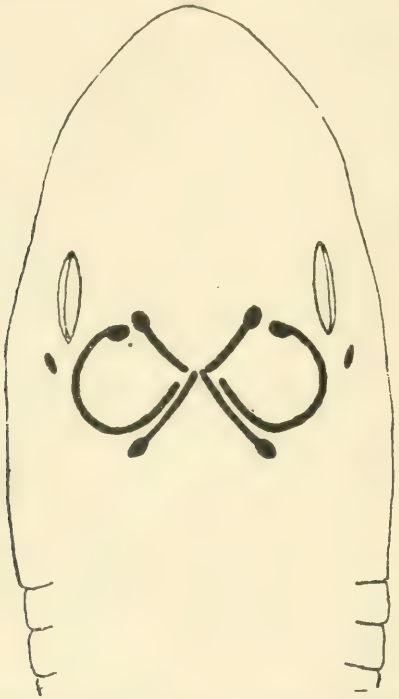
sinus utriculi superior. The plane of the anterior canal is not precisely a vertical one, but in the normal resting position of the animal usually inclines laterally in descending. The angle of inclination is very different for different individuals; actual measurements in two specimens give a value of 1.5° and 7°. The term "sagittal," so often applied to this canal, is a decided misnomer in the present species, inasmuch as the canal plane forms a large angle with the true sagittal plane of the body (35° in one specimen, 43° in another). (Fig. 1.) The external canal bends strongly but gradually upward at its posterior end. With this exception its plane extends laterally, usually in a true horizontal direction; in passing anteriorly it dips from the horizontal plane (11° in one specimen, 15° in another). The posterior (vertical) canal, as always in sharks and rays, forms a complete ring, that communicates by a side opening (*ductus canalis posterioris*) with the postero-median portion of the *sacculus*. Upon the wall of this duct lies the *macula acustica neglecta*, which bears no otolith. The canal bears its ampulla on its lowermost outer portion. Its plane is approximately a vertical one. Careful measurement in one specimen showed an inward inclination of 0.5° in descending, in another an outward inclination of 2°. In extending posteriorly, it is inclined outward from the sagittal plane of the body to a varying extent (37.5° in one specimen, 40° in another), forming with the anterior canal of the same side an angle of something more than 90° (Fig. 1). Its occasional name of "frontal" is entirely inapplicable. For physiological reasons it is interesting to notice, that its relations to the body planes are almost exactly the same as those of the anterior canal of the opposite side.

The *ductus endolymphaticus* extends from the antero-median portion of the saccule upward through the perilymphatic cavity, to the median side of the utricle, pierces the cartilaginous roof of the auditory capsule, the sub-cutaneous tissue and the skin, and opens by a small pore to the outside. Through it the saccule and hence the whole membranous labyrinth are in free communication with the exterior. It contains a small quantity of otolithic matter.

The acoustic nerve enters the auditory capsule through its own foramen and separates at once into two main divisions, *ramus anterior* and *ramus posterior*. The former gives origin to three branches, *ramulus recessus utriculi*, *ramulus ampullæ anterioris*, and *ramulus ampullæ externæ*, supplying respectively the *macula acustica* of the utricular recess, the *crista acustica* of the anterior ampulla, and the *crista acustica* of the external ampulla. From the *ramus posterior* come off the *ramulus sacculi*, *ramulus neglectus*, *ramulus lagenæ*, and

ramulus ampullæ posterioris, supplying respectively the *macula acustica* of the saccule, the *macula neglecta*, the *papilla acustica lagenæ*, and the *crista acustica* of the posterior ampulla. The three ampullar branches are fairly compact, the others are more diffuse.

FIG. 1.



Dorsal view of anterior portion of body of dog-fish to show position of semicircular canals. Diagrammatic.

At the outset it was decided to exclude the rough and uncertain experiment of cutting the canals. The methods actually employed, in testing the functions of the various parts, were of three kinds, viz. stimulating the nerve endings, and throwing out of function the end-organs by cutting the auditory nerve or its branches, or by removing the otoliths. The walls of the auditory capsule being cartilaginous, it is easy with very little bleeding to reach almost any part of the ear. The cutting was usually done from above, the perilymph cavity being laid open more or less, according to the end desired. Because of the presence of the fluids in the cavities, it was thought that mechanical stimulation was more exact than electrical, hence the latter was not

employed. Stimulation was effected by pressing with a blunt needle, or a bit of cotton wool, directly upon the part to be tested—in the case of the membranous ampullæ, upon their surfaces, in the case of the vestibule, upon the otolithic masses. The nerve endings are very responsive and the slightest touch often brings out the reaction. It was found easy to cut the auditory nerve within the capsule and this was the method usually adopted, when the whole nerve was to be severed. In a very few cases, for special purposes the nerve was cut within the cranial cavity. It was definitely proved that the mere fact of opening this cavity did not prejudice the conclusions that were drawn from these few exceptional experiments. The nerve branches supplying the ampullæ were cut very readily, those of the anterior and the external within the perilymph cavity just at the entrance of each into its membranous ampulla, that of the posterior, within its own cartilaginous channel at a little distance from its ampullar ending. It was found impracticable to cut the nerves supplying the otolithic portions without great injury to the membranous labyrinth. Accordingly it was sought to throw out of function these parts by removal of the otoliths themselves. This somewhat less exact method was accomplished by unroofing the vestibule and, after breaking up the otolithic masses with forceps, washing out the contents by a fine stream of sea-water from a wash-bottle. Such a procedure had the apparent disadvantage of replacing the endolymph with sea-water, but it must be remembered that the endolymphatic duct has the cutaneous opening already referred to. The composition of endolymph must hence closely approximate, if not be practically identical with, that of the surrounding medium.

During the operation the animal was out of water, attached to a "shark-board," devised for the purpose. This consisted of a long, narrow flat board, on which the fish lay, covered closely by a wide-meshed piece of fish netting, which was attached firmly to the edges of the board. A rubber tube conveyed sea-water from the laboratory supply to the animal's mouth, from which the water ran constantly over the gills and out of the gill-slits. In this way respiration was insured and it was possible to keep the animal without detriment or discomfort upon the table for any desired length of time. The operation could thus be performed with entire deliberation. Warned by the work of some other experimenters, the greatest care was exercised constantly that the surgical work be done exactly and with a full understanding, at the time, of what was taking place. To guard further against unwarrantable inferences, no experiment was accepted as

conclusive or pertinent, until a post mortem examination had revealed the actual morphological results of the operation. After each operation the skin wound was sewed up, and the animal was returned to his aquarium and finally to a commodious car several feet deep floating in the sea-water. Here he was kept for days and his actions were studied frequently. The inconclusive results, obtained by some others in this field, seem undoubtedly to be due to lack of sufficient care, first, in performing the operations, and secondly, in maintaining the animals for after study.

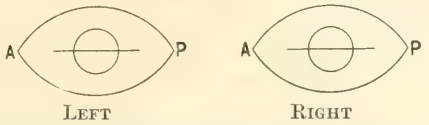
III. Compensating Movements.

The necessity of a suitable index of the state of equilibrium of the body at the moment of observation is obvious. As is well known, when a living animal is thrown out of his normal position, he makes certain involuntary movements, particularly of the eyeballs and limbs. The evident object of the latter is to counteract the outside influence and to return the body to its customary attitude. The eye movements are an indication of the efforts of the animal to retain the optical sensations customary to the normal position. Breuer (1875) gave the name "compensirende Bewegungen" to such movements. Compensating movements of the eyeballs and fins are well marked in the dog-fish and it is necessary now to turn our attention to a study of these.

A few words of anatomy by way of introduction. The fins of the dog-fish are eight in number, four paired and four unpaired. The two large pectorals project normally 20° to 45° ventro-laterally from the ventro-lateral aspect of the body opposite the posterior gill slits. The two pelvics are much smaller and less mobile and are situated about midway of the length of the body on its ventro-lateral aspect. Halfway between them and the tip of the tail in the mid-ventral line is the single small and comparatively unimportant anal fin. In the mid-dorsal line are the anterior and posterior dorsal fins, the former large, mobile and occupying the space opposite the interval between the pectorals and pelvics; the latter, smaller and stiffer, lying opposite the anal. The irregular caudal fin extends for a considerable distance along the dorsal and ventral median lines but consists of short fin rays only slightly movable in themselves. The power of the fins to make compensating movements diminishes in an antero-posterior direction, the most delicately responsive and the most contractile ones being the two pectorals and the anterior dorsal. Even these, however, do not in these respects equal the eyeballs. More attention was hence paid to

the movements of the latter. In the normal resting position the eyes look laterally (Fig. 2); in compensation they may be turned upward or downward, forward or backward, or may be rotated about their visual axes.

FIG. 2.



LEFT RIGHT

Normal resting position of eyes. *A* = anterior pole; *P* = posterior pole. The left eye is represented as seen from the outside, the right as seen from the median side. The straight lines indicate the true horizontal plane of the eyeballs. All subsequent figures are constructed upon the same plan as Fig. 2.

In the following experiments, continuous rotation was never tried, the object being not to study the phenomena of dizziness but the simple results of throwing the body suddenly out of equilibrium about any one of the three chief body axes, the longitudinal, the vertical and the transverse. Rotation about other axes was not studied, as such movements are compound ones, always capable of resolution into elements involving at least two of the chief axes. For example, rotation in the plane of a vertical semicircular canal always involves rotation about the longitudinal and transverse axes. The normal resting position of the fish is of course that in which the longitudinal and transverse axes are horizontal, the dorso-ventral axis vertical, the back upward, the belly downward. If the animal be held in the hands in this position, either in the air or water, and then be turned suddenly a few degrees about any one of his axes, the following phenomena may be observed:

1. When rolled about the longitudinal axis,

(*a*) to the left:

Left eyeball rolls straight upward.
Right " " downward.
Left pectoral and pelvic fins bend strongly downward.
Right " " " upward.
Dorsal fins bend strongly to the left.
Anal fin bends slightly to the right.

It is seen that the eyes and fins rotate in opposite directions as regards the longitudinal axis of the body, the eyes in a direction opposed to that of the body movement (or, when looked at from behind, with the hands of a watch), i. e., for the purpose of maintaining the sensations of the resting position; the fins in the same direction

as the body movements (or contrary to the hands of a watch), i. e., to resist the change of position. It is a fact of great interest and importance that the compensating positions are maintained as long as the animal is held upon his side. This indicates conclusively that while he continues in his new position, a constant stimulus is being applied to his equilibrium organs; i. e., in the process of turning him upon his side and keeping him there, both dynamical and statical organs are brought into action. It should be remembered that all the phenomena here mentioned are marked in a diminishing ratio in the eyes, the large pectoral and the anterior dorsal fins, and the more posterior appendages. (Fig. 3.)

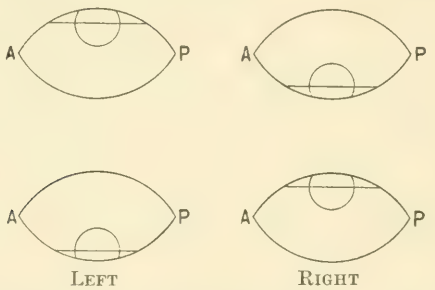
(*b*) to the right:

The movements are just the reverse of the above, viz.:

Left eyeball rolls straight downward.
Right " " upward.
Left pectoral and pelvic fins bend strongly upward.
Right " " " downward.
Dorsal fins bend strongly to the right.
Anal fin bends slightly to the left.

The maintenance of the positions is the same as in 1 *a*. (Fig. 3.)

FIG. 3.



Compensating positions of eyes for body positions 1 *a* (upper figures), and 1 *b* (lower figures).

2. When rolled about the vertical axis,

(*a*) to the left:

Left eyeball rolls straight forward, i. e. anteriorly.
Right " " backward, i. e., posteriorly.
Paired fins do not move.
Dorsal fins bend to the right.
Anal fin bends to the left.

The new positions are maintained only during the movement, both

eyes and fins returning to their normal places as soon as the body comes to rest, i. e. here dynamical organs are alone brought specially into function. (Fig. 4.)

(*b*) to the right:

The movements are reversed:

Left eyeball rolls straight backward.

Right " " forward.

Paired fins do not move.

Dorsal fins bend to the left.

Anal fin bends to the right.

The maintenance is as in 2 *a*. (Fig. 4.)

3. When rolled about the transverse axis,

(*a*) the head lowered:

Left eyeball rolls its anterior pole upward.

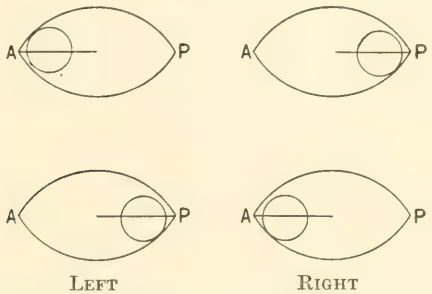
" " posterior pole downward, i. e. rotation about its visual axis.

Right eyeball rolls similarly.

All paired fins bend dorsalward.

Median fins do not move.

FIG. 4.



LEFT RIGHT

Compensating positions of eyes for body positions 2 *a* (upper figures), and 2 *b* (lower figures).

As in 1 *a* and 1 *b*, the new positions of eyes and fins are maintained while the body is held in its abnormal attitude. (Fig. 5.)

(*b*) the head raised:

The movements are reversed:

Left eyeball rolls its anterior pole downward.

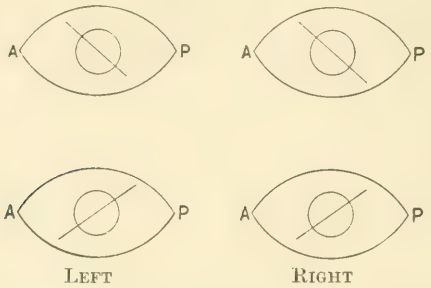
" " posterior pole upward.

Right eyeball rolls similarly.

All paired fins bend ventralward.

Median fins do not move.
The maintenance is as in 3 *a*. (Fig. 5.)

FIG. 5.



Compensating positions of eyes for body positions 3 *a* (upper figures), and 3 *b* (lower figures).

4. When rolled simultaneously about two axes:

The compensating movements are always a combination of the movements accompanying rotation separately about the same axes.

All the above-mentioned compensating movements are evidently reflex actions, that are produced through afferent impulses affecting the centres for the contraction of the eye and fin muscles. Our next inquiry shall be concerning the sensory end-organs of the reflex arc.

IV. The Acoustic Nerve.

As Loeb has already pointed out, cutting the acoustic nerve of one side produces well-marked and constant statical and dynamical effects. As regards the statical phenomena, within a few minutes the eyeball of the operated side becomes deflected slightly downward. The deflection increases until, before an hour has passed, the visual axis may be inclined 20° to 40° downward from the horizontal and at the same time turned slightly posteriorly. The eye of the opposite side in the meantime turns to a less degree upward and slightly forward. The pectoral and pelvic fins of the operated side are deflected dorsalward from the normal so that they come to project from the body more nearly in a horizontal plane, while the corresponding fins of the opposite side are bent more ventralward than the normal. The dorsal fins, especially the anterior one, are bent away from the operated side, the anal fin slightly toward this side. That is, looked at from behind, in the case of section of the right auditory nerve the eyes are misplaced in the direction of the motions of the hands of a watch (plus the slight obliquity) and the fins in the opposite direction, and vice

versa with section of the left. The abnormal positions are permanent (at least for two weeks, which is the longest time that an operated animal has been kept alive and studied). These results are the same as those obtained in the study of compensating movements by turning the animal's body about the longitudinal axis into the positions 1 *a*, or 1 *b*. (Fig. 3.) Cutting the left auditory nerve, for example, displaces the eyes and fins in exactly the same manner (except the slight antero-posterior displacement of the former), as turning the normal body about the longitudinal axis to the right and holding it there. Is it unreasonable to believe that essentially the same sensations prevail in the two cases? In the case of passive rotation, the displacement of the parts continues as long as the sensations of abnormal position continue; in the case of cutting the nerve, may not the permanent displacement of the eyes and fins be regarded as evidence that the sensations of rotation to the right are permanently present? The paired fins of the operated side are held slightly closer to the body than those of the opposite side. Along with the changes in the positions of the organs mentioned, the whole body of the fish is curved markedly to the operated side and reclines to a slight extent upon this side. If the animal be seized by the hand in the water, he struggles to free himself, like a normal fish. He resists attempts to turn him upon his uninjured side, but usually becomes quiet as soon as the operated side is turned downward. This is often very marked.

As regards the dynamical effects following section of the acoustic, the most common one is the production of beautiful rolling movements toward the operated side about the longitudinal axis accompanying forward progression. A few rolls often occur at once after the operation, when the animal is returned to the water, but usually he remains for a time rather sluggish and rolls persistently only after the lapse of a few hours. Normal progression seems always possible; though even in this case there is a tendency to a depression of the operated side, the animal swimming with this side lowered often 10° to 20° from the horizontal. But, often of his own accord and almost invariably upon stimulating him to quick movements, the rolling begins and accompanies the onward progression, it may be for two or three minutes, before he finally comes to rest in the customary attitude upon the bottom of the car. After ten operations on dog-fish and five upon skates, the rolling was absent in no case in the former, and in one only in the latter, this skate being very much exhausted by the operation and surviving it less than four hours. Skates sometimes roll without onward progression and with their longitudinal axis almost vertical in

the water. This has not been seen in sharks. The animals retain the rolling power throughout life. Occasionally there is a tendency toward circus movements, i. e. about the animal's vertical axis, toward the operated side, but this has never appeared preeminent. Somersaults, i. e. turning about the transverse axis, have never been seen, nor, according to the theory that will be developed later, ought they to occur. The compensating movements of the eyes and fins are still possible in all three planes, after one acoustic nerve is cut, but they are much weakened and sometimes difficult to observe. In studying them, it must be remembered that the parts in question are already out of their normal position and the compensating efforts result mainly in increasing or diminishing the abnormalty. The presence of one acoustic with its end-organs, however, seems all that is necessary to the carrying out of the movements themselves.

Cutting both acoustic nerves causes no abnormality in the position of either eyes or fins and no curving of the resting body. Statical equilibrium, however, seems very completely done away with. The animal may be placed upon his belly, his back, or either side without manifesting objection, and, after swimming, he may come to rest in any one of these positions. In reclining, he is perhaps most easy in his customary resting position with belly downward, yet he does not appear to be seriously inconvenienced by any other attitude, and, when supported by the side of the tank, has been seen to rest standing upon his head. Dynamically also he lacks equilibrium. He may, it is true, swim in his normal manner, but he swims with almost equal readiness upon his back or even upon his side. He may roll about his longitudinal axis to either side, or make circus movements about the vertical axis. No one kind of movement continues long, the swimming being very irregular. Compensating movements are entirely done away with, although the animal is able voluntarily to move his eyes and fins. The only justifiable inference is that, in cutting the acoustic nerves, we have separated from the brain the sense-organs that mediate the afferent impulses of the reflex compensating act.

In brief, then, section of one acoustic nerve interferes to some extent with both statical and dynamical equilibrium, by causing an abnormal position of the trunk, the eyes and the fins, and forced movements; but compensation is still possible. Section of both acoustics destroys much more completely the sense of both statical and dynamical equilibrium, even to the extent of doing away with the compensating power.

These phenomena of the cut acoustics may be explained with entire

satisfaction by the theory—and, it seems to me, only by the theory—that the fibres of the acoustic nerve supply the leading end-organs of the senses both of statical and of dynamical equilibrium. Each acoustic with its organs is preeminent for its own side of the body, and, in the normal resting position, mediates preeminently the normal statical sensations of its own side. If the body be turned out of its normal position toward one side and be maintained in a new position, the acoustic of that side preeminently mediates the accompanying dynamical and statical sensations. But the other acoustic functions at the same time to an appreciable, though a less, extent. Hence each nerve possesses a principal and a subordinate equilibrium function, the former dealing with motions toward the side of the body on which the nerve lies and the corresponding resting positions, the latter with motions toward the opposite side and the corresponding resting positions. Cutting one nerve leaves the animal to be guided only by the unbalanced sensations communicated from the other side. The result may easily be that, in resting in the normal position, he has the illusion of a depression of the uninjured side, as though it were overweighted. This causes an actual compensating depression of the operated side, and corresponding compensating displacements of the eyes and fins; when held in the hand, he is most quiet with the operated side turned downward. If he attempts to swim, there is an analogous lack of balance in his dynamical sensations; he feels that his body is being rotated toward the uninjured side; to prevent which, an actual "forced" movement of rotation toward the injured side occurs. Theoretically, this rotation may be either in a vertical or a horizontal plane, i. e. about the longitudinal, or about the vertical axis; as a matter of fact, in my own experiments the former has been most pronounced. Further, since each nerve has a subordinate, as well as a principal function, normal compensation of the eyes and fins is still possible. Cutting the other nerve, however, equalizes the matter once more. There is no longer a lack of balance of the equilibrium sensations. The leading ones are entirely wanting. The animal doubtless gets some help from optical, tactile, muscular and perhaps other sources. The body is righted and straightened, the eyes and fins assume their normal positions, normal body position and progression are, as always, possible, but the fish is nearly as well satisfied to rest upon his back or his side as upon his belly; and, in swimming, irregularity is as frequent as, or more frequent than, the reverse. Compensation is no longer possible.

So far the facts and their explanatory hypothesis in gross. We

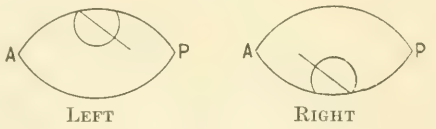
ought to go much farther than this, however, both in the analysis of the facts and in the completeness of their explanation. For this, we must turn to experiments upon the various branches of the acoustic nerve and learn whether it is not possible to localize in definite parts of the ear the functions in question.

V. The Semicircular Canals.

1. *The anterior canals.*

Stimulating the ampulla of one anterior canal causes the eyeball of the same side to roll upward, the anterior pole somewhat more than the posterior, so that the eye, while as a whole being turned upward, becomes rotated obliquely about the visual axis; at the same time the opposite eye rolls downward, the posterior pole more than the anterior, hence also taking an oblique position (Fig. 6).

FIG. 6.

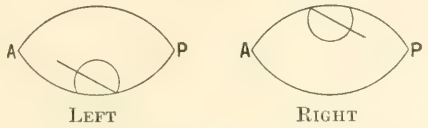


Position of eyes upon stimulation of the left anterior ampulla.

These movements are evidently combinations of the normal compensating movements, obtained by turning the body in the sagittal and the transverse-vertical planes, and are exactly what would be expected to result from movement of the normal body in the plane of the canal, whose ampulla is stimulated. For example, turning the normal body about the transverse axis, head downward (position 3 *a*), causes the left eye to become oblique with the anterior pole upward, the posterior pole downward, the right eye taking a similar position (Fig. 5); turning about the longitudinal axis to the left (position 1 *a*) causes the left eye to roll upward, the right eye downward (Fig. 3). Turning the body about both the axes at once, i. e. in the plane of the left anterior canal, must cause a combination of the rolling and the obliquity of each eye, and that is exactly what is seen when the left anterior ampulla is stimulated. The same reasoning may be applied to the fins, for stimulation of one anterior ampulla causes the paired fins of the same side to bend slightly downward, those of the opposite side strongly upward, the dorsals to the stimulated side.

Stimulating both anterior ampullæ simultaneously was not tried. But the results may readily be inferred. Left stimulation causes the positions shown in Fig. 6, right stimulation those in Fig. 7.

FIG. 7.

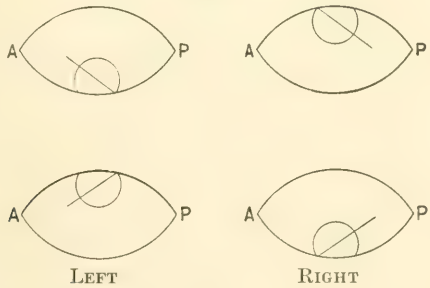


Position of eyes upon stimulation of the right anterior ampulla.

Hence, with bilateral stimulation, the vertical element in the movement would be eliminated and the obliquity alone would remain, i. e. exactly the condition of things with the normal animal in position 3 *a* (Fig. 5) and, as we shall see, the permanent position of the eyes of the fish both of whose posterior ampullar nerves are cut (Fig. 12).

Cutting the nerve of one anterior ampulla may cause to a slight extent the same abnormal resting positions of eyes and fins and trunk that cutting the whole acoustic causes. But all such abnormalities are uncertain in their appearance and not continuous. The animal swims normally and well. No forced movements are ever seen. Compensation is well marked and normal, with one interesting exception. In position 3 *a* the eye of the operated side, while taking the normal oblique position, becomes also rolled somewhat downward, the opposite one somewhat upward. In position 3 *b* the reverse movement takes place (Fig. 8).

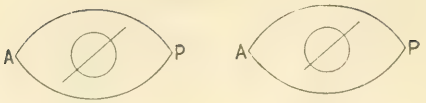
FIG. 8.



Compensating positions of eyes for body positions 3 *a* (upper figures), and 3 *b* (lower figures), after section of the left anterior ampullar nerve.

Cutting both anterior ampullar nerves causes the two eyes to become oblique, their anterior poles being depressed, their posterior poles elevated (Fig. 9).

FIG. 9.



LEFT RIGHT

Resting position of eyes after section of both anterior ampullar nerves.

It will be noticed that this is exactly the same result as that obtained by placing the normal animal in position 3 *b* (Fig. 5). There is a marked tendency on the part of the animal to remain upon the bottom of his tank and a great disinclination to rise up to the surface of the water or to be held horizontal in the hand. If this latter be done and he then be set free, he at once dives with head downward striking the bottom with the tip of his nose and then coming to rest on the horizontal floor, or swimming about close to it, probably with guiding sensations obtained by touching the bottom. This movement is very pronounced and characteristic. It must be regarded as a true forced movement, entirely analogous to the rolling after section of one acoustic. The compensating movements appear somewhat weak, irregular and indefinite. They seem to be normal for positions 1 *a* and 1 *b*, 2 *a* and 2 *b*, and 3 *b*. For 3 *a* they are usually entirely wanting.

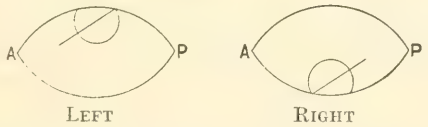
The results of stimulating and of cutting the anterior ampullar nerves justify the inference that their canals are the functional dynamical organs in rotations forward and downward about the transverse axis of the body and in all compound movements in which this is one of the component elements. Each canal is in most complete activity, when the movement is in its own plane and in the direction of its ampulla (*Cf.* Fig. 1). The nerve endings are stimulated by the endolymph flowing through the ampulla from the *utriculus* toward the canal. In all forward rotational movements in vertical planes lying between the planes of the two canals, the latter function together as a double organ; in the true sagittal plane, they act to an equal degree; in all planes lying between the sagittal plane and the plane of either canal, the canal of that side is functionally predominant over the other. Throwing out of function one canal does not seriously interfere with the actions of the individual—the interesting alteration of eye compensation for position 3 *a* will be discussed later. But bilateral nerve section removes an important link from the chain of equilibrium sensations, destroys the compensating power of the eyes for movements once appreciated by the now useless canals, and leaves the posterior canals only to deal with vertical rotational movements. As we shall see later,

the chief function of these organs is the reverse of those under discussion, viz. the appreciation of backward movements about the transverse axis. With these only in function, the fish feels all movements about this axis to be more or less in a backward direction; when disturbed, he has the sensation of backward tumbling. To counteract this, the eyes compensate and he makes the characteristic "forced" forward dive.

2. *The posterior canals.*

The results here obtained are entirely analogous to those just discussed. Stimulating the ampulla of one posterior canal causes the eyeball of the same side to roll upward, the posterior pole moving farther than the anterior, so that, together with the upward movement, there is obliquity about the visual axis; the opposite eye rolls downward, the anterior pole more than the posterior, hence also an obliquity in the same sense (Fig. 10).

FIG. 10.

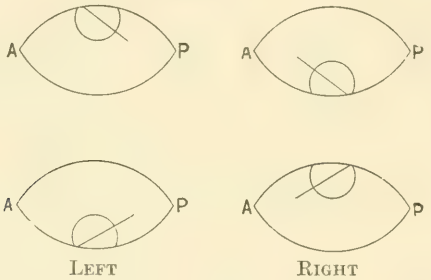


Position of eyes upon stimulation of the left posterior ampulla.

As with anterior stimulation, we have here also a compound movement, made up of a vertical and an oblique element. If, as in the figure, the operation be performed upon the left side, the vertical element is that of the normally compensating animal moved into position 1 *a* (Fig. 3); while the oblique element is that of the animal in position 3 *b* (Fig. 5). But movements 1 *a* and 3 *b* performed simultaneously are equivalent to a backward rotation of the trunk in the plane of the left posterior canal. Hence it follows that the function of this canal, like that of the anterior, is the appreciation of movements in its own plane toward its ampulla, the stimulus arising likewise by the endolymph rushing through the ampulla toward the canal proper. The fin movements resulting from unilateral stimulation harmonize with this view—the paired fins of the same side downward, of the opposite side upward, the dorsals to the side stimulated. The posterior canal may hence be called the functional opposite of the anterior canal of the other side. Lying essentially in the same plane, the two appreciate rotations in the same plane but in opposite directions. Stimulation of both posterior ampullæ together would doubtless

neutralize the vertical element in the above eye movements and cause those of position 3 *b* (Fig 5)—a result also produced, as we have already seen, by cutting the nerves of the two anterior ampullæ. We must hence infer that in all backward rotations of the body in the sagittal plane the posterior canals are the functional ones and the functional opposites of the anterior. Cutting the nerve of one posterior ampulla has so far not been seen to cause statical abnormalities. In his usual movements too the animal seems entirely normal. Compensation in position 1 *a* and 1 *b* and 2 *a* and 2 *b* appears normal and strong. But in 3 *a* and 3 *b* there are modifications, entirely analogous to those observed in the exclusion of one anterior canal; for example, in 3 *a* the eye of the operated side compensates normally but at the same time rolls upward, the opposite eye also normally but with a downward roll; in 3 *b* exactly the reverse takes place (Fig. 11).

FIG. 11.

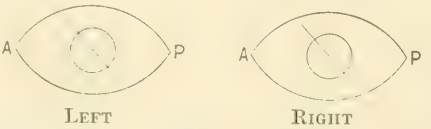


Compensating positions of eyes for body positions 3 *a* (upper figures), and 3 *b* (lower figures), after section of the left posterior ampullar nerve.

These compensations are the same as those seen after cutting the anterior ampullar nerve of the opposite side, the significance of which fact will appear later.

The phenomena that follow section of both posterior ampullar nerves, present also interesting analogies to those following anterior section. The two eyes are oblique but with their anterior poles raised and their posterior poles depressed (Fig. 12).

FIG. 12.



Resting position of eyes after section of both posterior ampullar nerves.

It will be seen that this is the same position as in 3 *a* of the normal animal (Fig. 5). While the lack of functional anterior canals causes the animal to dive downward, the cutting of the posterior nerves causes quite the reverse. When returned to the water after the operation, the fish is very uneasy, but disinclined to swim deeply; he remains near the surface, at times thrusting the head far out of water and turning backward, as if endeavouring to turn backward somersaults. Later he becomes more quiet, yet, if depressed beneath the surface, always tends to shoot upward, thrust the nose out of water and swim continuously with the body nearly vertical, the head upward and the tail downward. A completely vertical position is often reached, and is sometimes surpassed so that the dorsal surface is turned actually slightly downward. This upward and backward movement with anterior canals intact, is to be contrasted with the downward, forward dive of the fish, which possesses only his posterior canals. Both are true forced movements, the one being the counterpart of the other. Compensation is apparently normal in all positions, except 3 *b*, where it is usually wholly wanting. These results indicate that a fish with functionless posterior canals has the sensation of a constant tumbling forward, hence the compensating backward movements. We might indeed use exactly the same language regarding the function of these canals that we have used on page 330 with reference to their anterior counterparts, substituting only the words posterior, anterior, backward, and forward respectively for "anterior," "posterior," "forward," and "backward." Each posterior canal functions most completely in backward rotations in its own plane; each pairs with its fellow in rotational movements in planes lying between the two. These canals are in all senses the exact functional counterparts of the anterior pair.

3. *The anterior and posterior canals combined.*

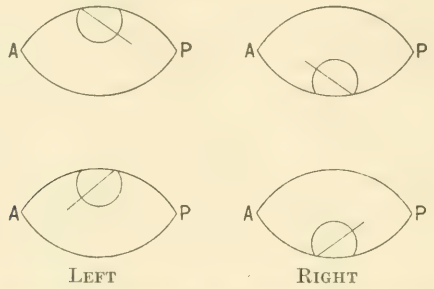
The effects upon the eyes of stimulating the anterior and the posterior ampullæ have already been given. For left stimulation they are shown again in Fig. 13.

Stimulating both together would probably eliminate the obliquity and give the position represented in Fig. 14, i. e., the same as normal compensation in position 1 *a* (Fig. 3).

It would seem, then, that when the normal animal is turned about his longitudinal axis, the anterior and posterior canals together mediate the sensations and preeminently those canals of the side toward which the movement takes place. That is, just as in rotations in the sagittal plane there is a pairing of anterior canal with anterior and of posterior

with posterior, so, in rotations in the frontal plane, there is an analogous pairing of left anterior with left posterior and of right anterior with right posterior. Each lateral vertical pair has likewise its functional opposite. In movements in the true frontal plane the two canals

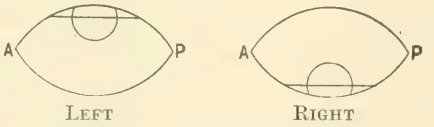
FIG. 13.



Positions of eyes upon stimulation of the left anterior ampulla (upper figures) and the left posterior ampulla (lower figures).

of the same side act to an equal degree. As the plane of rotation approaches more nearly that of the anterior canal, the latter becomes functionally more important and finally all important, when the two planes coincide: and vice versa for the posterior canal. The effect of cutting the nerves of these two canals was studied in several sharks with interesting results, viz. tendency of the body to recline with the operated side somewhat downward, the eye of this side strongly downward (usually also with a slightly posterior position), the opposite eye

FIG. 14.



Presumed position of eyes upon simultaneous stimulation of the left anterior and posterior ampullæ.

strongly upward (and slightly forward); the fins bent in the direction opposite to the eye displacements; in swimming, tendency to keep the operated side somewhat downward, often passing into typical continued rolling movements toward this side. Compensation in all positions is possible, though usually not so strong as in the normal animal. When held in the hand, the fish may easily be turned about the longitudinal axis toward the operated side but resists turning in the opposite direction.

These results are entirely analogous to those of bilateral anterior or posterior ampullar nerve section, and confirm the above deductions regarding the pairing of the two vertical canals of the same side in rotations about the longitudinal axis. They also furnish the key to many of the phenomena following section of the acoustic nerve. The latter phenomena comprise all of the former. Inasmuch as this is the case, the deduction is not only justified but is inevitable that these constituents of the whole result of acoustic section are to be referred to the anterior and posterior ampullar components of that nerve. The parallelism of effects is bilateral as well as unilateral. The nerves of all four vertical canals were cut, leaving the horizontal canals and vestibular parts intact and functional. In this state, at rest the eyes and fins are entirely normal in position; they are capable of normal movements; compensation is still possible in position 2 *a* and 2 *b*, i. e., in horizontal rotations, but is entirely wanting in positions 1 *a* and 1 *b* and 3 *a* and 3 *b*, i. e., in all vertical rotations. The animal may swim normally, but at times shows beautiful continuous rolling about the longitudinal axis to the right side or to the left. His dynamical equilibrium as regards vertical rotations seems very much disturbed. His statical equilibrium is in general good, although occasionally after swimming he has been seen to settle down upon his back or his side.

Lastly, some interesting facts were brought out by diagonal operations upon the vertical canals. Simultaneous stimulation of the anterior ampulla of one side and the opposite posterior would probably cause no movement of the eyes, the tendencies toward movement being in opposing directions and hence neutralizing each other. The effects of section of two such nerves have been actually observed and are as follows: a strong tendency toward a lateral bend of the trunk of the body, manifested at times by jerking from side to side; at rest no very marked abnormality of eyes and fins (in the most successful case, where the left anterior and the right posterior were severed, the eyes and fins manifested a slight tendency toward the abnormalities of the single cut anterior); in movement a swaying from side to side about the longitudinal axis, amounting even to an occasional half roll or a complete rolling over; no continuous rolling movement, as in the case when the two verticals of the same side are cut. The compensating power of such an animal is normal for positions 1 *a* and 1 *b* and 2 *a* and 2 *b*; for positions 3 *a* and 3 *b* it is exactly what it would be, if either nerve alone were cut, but the effect is more intense, the eyes, while compensating as in a normal fish, moving strongly upward or downward as the case may be (See pages 329, 332). This at first sight strange result

appears to contradict our theory of the functions of the canals. In reality it enables us to perfect and complete it. To explain the facts, we must refer back to the experiments already detailed. Why, for example, if the view already stated of the combined action of the two posterior canals be correct, do not the eyes of a fish, whose left anterior ampullar nerve alone is severed but both of whose posterior ampullar nerves are still functional, compensate in position 3 *b* entirely like a normal animal? (See Fig. 8, lower figures.) Evidently not alone do the posterior canals act in backward sagittal rotation. Similarly, the result represented in Fig. 11 (upper figures) shows conclusively that likewise in forward rotations the anterior canals are not the sole signalling organs. In fact we are forced to the conclusion that, when any one canal or pair of canals is acting, its functional opposite is also acting. In other words, just as each acoustic nerve has a principal and a subordinate function, so has each ampullar branch of the acoustic. The principal function is the transmission of impulses of rotations in the plane of its canal toward its ampulla, the subordinate is the transmission of impulses of like rotations in the opposite direction, or away from its ampulla. The former is called into action by the flow of endolymph through the ampulla into the canal, the latter by the flow in the opposite direction. The principal function of one vertical ampullar nerve, or ampulla, or canal is the same as the subordinate function of that diagonally opposite—in other words, the functional opposite; hence if both nerves be rendered functionless, the effects are more intense than with one. This principle of a double function likewise pertains to the organs when functionally paired, the principal function of each pair being the same as the subordinate of the functionally opposite pair. The idea of a double function for each ampulla is not a new one. It has been discussed and experimentally verified by Breuer and others for higher animals, and is essential to the interpretation of the facts. It necessitates the hypothesis of two functionally different kinds of nerve endings in the *crista acustica*. It may be asked, why do we not, then, in the fishes, upon stimulation of the ampulla obtain motor reactions, indicating a subordinate function? I reply that, so far, this point has not been studied experimentally. My own method has been to stimulate the ampulla as a whole; and the fact that the subordinate reactions have never been obtained proves of itself only that, if two functions are localized there, one must be subordinate to the other. I shall hope later to bring forward conclusive experimental proof of the presence of both.

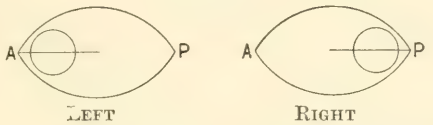
We here leave the discussion of the vertical canals. The mutual

bearings of the facts and the interrelationships of the organs are manifold and much might be said still along these lines. Enough has, however, been presented to illustrate clearly the principles, to which the facts lead us. The proof of the dynamical rotational function of the canals seems abundant. Their double function and their pairings enable the animal to appreciate all vertical rotations whatsoever. Horizontal movements must next be considered.

4. *The external canals.*

Stimulation of the ampulla of one external canal causes the eyeball of the same side to roll straight forward, that of the opposite side straight backward (Fig. 15).

FIG. 15.



Position of eyes upon stimulation of the left external ampulla.

The dorsal fins bend away from the side stimulated, the paired fins do not move. These movements are the same as those of normal compensation in position 2 *a* (Fig. 4), and it follows that each external canal is called into action by horizontal rotations toward its own side of the body.

As regards the effect of cutting the external ampullar nerves, my records at present are incomplete. Cutting the nerve of one side does not necessarily affect the resting condition of the eyes or fins. The eyes have been seen to be in a position exactly the reverse of that produced by stimulation, but often they remain entirely normal. At times the body is curved toward the operated side. No definite dynamical results have been made out, although circus movements might perhaps have been expected. The compensation also seems normal, though at times apparently weak in positions 2 *a* and 2 *b*. In fact, so far as my few observations have gone, the animal appears usually quite normal. One external canal is evidently sufficient for both sides of the body. Stated in the language now familiar to us, each horizontal canal, or ampulla, or nerve has, like each vertical or the whole acoustic, two functions, the principal one dealing with rotations toward its own side, the subordinate one with rotations toward the opposite side. Cutting both external ampullar nerves introduces marked changes. No static abnormalities result. The

animal prefers to remain at rest on the bottom of the car or to swim quietly near the bottom, frequently in small circles to the right or to the left with the body kept horizontal, and turning often quickly and sharply. If touched upon the side of the head, he shoots quickly in a horizontal arc away from the object. Good typical circus movements may be present in the true horizontal plane; such an animal has also been seen to stand erect in the water, and for several seconds turn the most beautiful rapid somersaults to one side in a small vertical circle, i. e. in the plane of his own external canal. Compensating movements are normal and strong in all vertical planes, but in the horizontal plane they are entirely wanting, although the animal has the power voluntarily to move his eyes and fins in all directions.

The dynamical rotational function of the external canals is evident and needs no further discussion. The analogy with the vertical canals is very close. Each horizontal stands to the opposite one in the same functional relation as each vertical to the one diagonally opposite, in both cases the principal function of one being the same as the subordinate function of the opposite. As to the mode of normal stimulation, there is one difference. Since the ampulla is situated at the anterior end of the external canal, the direction of the endolymph current, that calls forth its chief activity, is from the canal through the ampulla toward the *utriculus;* the opposite direction calls forth the subordinate function; with the verticals, as has been seen, the case is exactly reversed. This seemingly curious fact appears to depend wholly upon morphological considerations and probably has no special physiological significance. The question of a possible pairing of the horizontal canal with either of the verticals has not been tested experimentally. Such a functional combination, however, goes without saying. In this way we fairly may suppose all rotations in antero-horizontal and postero-horizontal planes to be appreciated or, in other words, all rotations involving simultaneously the three chief body axes. Not only is the horizontal canal entirely analogous to either vertical in its mode of working (except the direction of the endolymph current), but the laws of pairing should hold good for the former as well as the latter. Just as each single vertical or horizontal canal, or each vertical pair, has its functional opposite, so should each antero-horizontal pair have its opposed postero-horizontal and vice versa, with opposed principal and subordinate functions.

One word regarding the phenomena of the cut acoustic nerve. As already stated, circus movements have occasionally appeared as a result of this operation. These undoubtedly have their origin in the

external ampulla of the opposite side. After this operation all horizontal movements stimulate only the uncut nerve of that ampulla. The sensations of rotation about the vertical axis to that side preponderate, resulting in a compensating rotation to the injured side. A similar explanation may suffice for the curved condition of the trunk always seen after acoustic section.

5. *All canals combined.*

If all the canals of one side be thrown out of function by cutting their nerves, the result is much the same as that after the whole acoustic is severed, viz., at rest slight statical effects manifested by the abnormal positions of the eyes and fins, curvature of the body toward the injured side, and tendency to recline with this side slightly downward: in movement the injured side is held somewhat downward in otherwise normal swimming, the fish often darting off upon this side. This tendency to depression passes sooner or later into genuine rolling about the logitudinal axis toward the operated side; the compensating power in all positions is present but weakened. So too the section of the nerves of all six canals causes, so far as has been observed, effects similar to those of section of both acoustics, viz. the eyes and fins are normal in position; the fish swims on his belly, back or side, and comes to rest in any one of these positions; after settling on his back or side he apparently tries to return to his normal position but finds it difficult or impossible to do so; compensation is wanting in all movements.

It might seem to be a question whether, in these last two experiments dealing with all canals upon one or both sides, as in other cases of ampullar nerve section, the animal's sense of statical equilibrium also is not really interfered with. Abnormalities of position are, it is true, often present, but from them to ascribe a statical function to the ampullæ would seem to be hasty and illogical. On the contrary, that they are capable of explanation by the undoubtedly existing abnormal dynamical sensations, I myself have no doubt. I believe the facts so far to show that the statical abnormalities resulting from section of the acoustic have a twofold origin—partly from the loss of true statical organs, partly from the loss of organs essentially dynamical. Without more experimental data, however, I would be loath to discuss this question. I may add that Breuer also derives in the higher animals the abnormal positions after acoustic section partly from ampullar and partly from otolithic sources. However this may be, there is no doubt whatever about the possibility of tracing to the various ampullar fibres of the acoustic all of the dynamical rotational phenomena, that are

mediated by the nerve itself. We have found the definite localization that we sought.

Further, all the possibilities of functional combination of the canals are not exhausted by the cases of pairing already cited. Whenever the body movement is such as to involve rotation at the same time about the vertical and either one of the two other chief body axes, it seems evident that three canals must function together as a triple organ, each acting for its own component of the whole movement. Thus the external may act with the two anteriors or the two posteriors or with the anterior and the posterior of the same side. The triple organ would have, like the single canal or the pair, its functional opposite; and the relations of the two as regards their principal and subordinate functions would be the conventional one. Thus all possible rotational movements that the fish's body is capable of, are appreciated, and we have in the semicircular canals of the ear one of the most beautiful and perfect mechanisms that are to be found in the animal body. Lastly, if we allow the presence in each *crista acustica* of a double organ with opposite functions, the doctrine of specific nerve energies receives new and powerful justification.

The facts, so far communicated, establish, it seems to me, the dynamical function of the semicircular canals in rotational movements. The effects of stimulating the ampullæ and the effects of severing the nerves are harmonious with each other with hardly a single exception, and probably with none that cannot be explained by careful observation. These effects too harmonize entirely with the facts of normal compensation. There can be no question here of possible injury to the brain substance accompanying the operation. The method of stimulating the ampullæ renders superfluous the hypothesis that it is solely the brain, and not the brain plus the semicircular canals, that mediates sensations of equilibrium in rotational movement. Cutting the nerves, instead of cutting the canals themselves, gives pure results. By it the peripheral organ, supplied by the nerve branch, is alone thrown out of function; interference with the brain is out of the question. Nor, as some have thought, does cutting stimulate; on the contrary, it paralyzes. Further, the results detailed are, with a few unimportant exceptions, absolutely certain to follow, if the operator has actually done what he proposed to do; and one familiar with the subject is able to predict with certainty the essential results of any of the operations. The fact that the canals are not in the three chief body planes, has been brought forward as an argument against the theory of their dynamical function. *A priori* this consideration seems

untenable and, in view of the important facts established regarding the combinations of the canals, becomes entirely without weight.

VI. **The Vestibule.**

Stimulation of the otolithic parts of the ear has not been entirely satisfactory. The results were found exceedingly variable. The utricle and the saccule are very responsive to mechanical pressure, the lagena apparently less so. Such stimulation brought forth in the same animal at different times the same eye and fin movements as follow stimulation of the anterior, or the posterior, or the external canal, or such as may result from combinations of the canals. On the theory that the otolithic organs are statical in function, such movements (at least the vertical ones) would not be unexpected, since it will be remembered that, in our study of normal compensating movements, for the vertical changes of position, the compensating changes in the eyes and fins were found to remain fixed during the continuance of the altered body positions. But it would also be expected that the experimenter would be able to determine a localisation of function within the vestibular parts. Indeed Breuer has endeavored to show by argument the high probability of as sharp a physiological division of labour between the utricle with its horizontally extended otolith, the saccule and the lagena with their otoliths vertically extended, as exists among the semicircular canals. So far, in the dog-fish at least, to prove this has not been possible, since all the above movements apparently may result from stimulation of either the saccule or the utricle. It is hoped that further work will clear up this point and, in view of that possibility, it is thought unnecessary here further to discuss the details already obtained.

As already stated, a satisfactory method of cutting the nerves supplying the *maculae acustica* has not yet been found. For throwing these end-organs out of function, resort was had to the removal of the otoliths—a device already tried by other investigators. It may be questioned whether this entirely accomplishes the object sought. Breuer's theory that the constant pressure of the otolithic mass upon the stiff hairs of the hair cells induces a constant stimulation, is undoubtedly correct, but even he believes that, in the change of body positions, the amount and direction of the tension is altered—the otolith is not absolutely fixed in position; it lies embedded in the soft matrix that unites the hairs and, as it is acted upon by gravity in directions varying with the altered body positions, the hairs are swayed with it, and the nerve stimulus varies accordingly. It is conceivable

that, even with the otolith removed, the hair cells still may be to a slight extent functional. Nevertheless, I do not consider that this constitutes a serious objection to the method. However this may be, the removal of the otoliths from the vestibule has given clearer results than the stimulation experiments. If they be washed out of one ear, all the statical abnormalities follow that accompany the cutting of the acoustic nerve, viz. the eye of that side is downward and slightly backward, the opposite eye is upward and slightly forward, the fins are rotated in the opposite sense, and there is a tendency in reclining to keep the operated side somewhat (e. g. 15°) downward (I have recorded no bending of the body to this side). Normal swimming is possible, but during this also the operated side is usually directed somewhat downward. When disturbed, the animal usually darts off upon this side. In coming to rest, he often loses his balance and sinks down flatly upon this side, never upon the other. The loss of statical equilibrium is often very marked in these various ways. Compensating movements are normal in all planes; forced movements are wanting. These two facts are of supreme importance, in view of the fact that the dynamical organs, the canals, are still functional. In some cases, several days after the operation, rolling movements have appeared, it is true. But in every such case the post-mortem examination has revealed a pathological condition of the canals, shewn by distension with blood, discolouration, etc., that must have prevented their normal action. It seems to be a fact, then, that in these results we have a clue to the statical abnormalities following section of the acoustic nerve, in so far as these are incapable of a dynamical (ampullar) explanation. This idea is strengthened by the results of removing the otoliths from both ears. When this is done, the eyes and fins are in their normal position; the fish may be easily turned upon his back, and remains quiet in this attitude, or swims off, gradually turning over into his customary attitude; he often swims upon his side; in coming to rest, he often settles upon his back or his side. No continuous forced movements occur but, when he is disturbed, not rarely he gives a single roll or makes a circus movement, due apparently to inability at once to obtain his normal state of equilibrium. Compensating movements are perhaps weakened but are not necessarily done away with, as is the case with fishes lacking all semicircular canals. Their persistence in vertical planes (positions 1 *a* and 1 *b*, 3 *a* and 3 *b*) is seen no longer, the compensation ceasing with the cessation of the body movement. The general impression that an observer gets from such a fish is that, if left to himself, he can maintain his equilibrium fairly well, but that he is easily thrown

out of it. The expressive words of a sea captain, who was watching such a shark, are highly applicable, "That fish lacks ballast." He is distinctly less abnormal than one, who has had both acoustic nerves severed, in that he can regulate his movements better. My results in this field agree in essentials with those already reported by Loeb. Removal of otoliths from a single *macula* alone, whether utricular, saccular or lagenar, has not been attempted.

The facts here reported concerning the vestibular parts of the ear, while not as detailed as those dealing with the canals, all point to the conclusion that in this part of the ear lie the organs for statical equilibrium. Interferences with movement do indeed follow removal of otoliths. But, since in the normal animal with every movement and hence with every change of dynamical sensations a change of statical sensations occurs, it would be strange if the entire lack of customary statical sensations should not carry with it some abnormalities of movement. This would be simply a case of correlated disturbance of function; and the inference would not be justified, that organs essentially statical in function were also in part dynamical. The conclusion, to which my own observations tend, has however nothing to do with the question of a possible further function of the otolithic organs in mediating sensations of onward progression. This subject was not considered at all in my experiments, and future work alone must decide it.

VII. Summary of Results.

For the convenience of the reader, the results are here reported in brief. I do not doubt that the essential facts may be found to apply to other and higher Vertebrate types. Indeed to a considerable extent this has already been done. But until the other types have been carefully and fully investigated in a comparative way along the lines laid down in this research, I shall not commit the folly of too hasty generalization. For the present, then, let the results and conclusions be regarded as applying only to the forms experimented with.

The ear contains the sense-organs of both the dynamical and statical equilibrium of the body—of the former, at least, in so far as it has to do with rotational movements. The sense-organs of such dynamical equilibrium are the semicircular canals with their ampullæ and *cristæ acustica*. Each canal has a principal and a subordinate function; the former is the appreciation of rotational body movements in its own plane and toward its side of the body; the latter is the appreciation of similar movements but in the opposite direction. Each canal has a functional opposite, the two lying approximately in the same plane,

and the principal function of one being the same as the subordinate one of the other, and vice versa. The functional opposite of the left anterior canal is the right posterior; of the right anterior, the left posterior; of the left external, the right external; and vice versa. Each canal is in most complete action when the movement is in its own plane. From this standpoint, movements in planes other than those of the canals may be regarded as compound movements, and may always be resolved into the simple movements in the planes of the canals. Such compound movements involve the activities of the several canals that are brought into function by the simple movements. Examples of such movements are rotations about the transverse axis of the body (in the sagittal plane), rotations about the longitudinal axis (in the frontal plane), and simultaneous rotations about the longitudinal and the vertical axes. In such movements the canals involved act together to form a double or a triple dynamical organ, endowed with a principal and a subordinate function. In the first of the three cases cited, the two anterior canals act together and the two posteriors; in the second, the left anterior and posterior act together and the right anterior and posterior; in the third, all three left canals act together and all three right. Like the single canals, each double or triple organ has its functional opposite; and the relations of the principal and subordinate functions of the two are the same as with the single canals. Thus the canals afford an apparatus for the mediation of the sensations caused by all possible rotational movements.

The stimulating agent of each end-organ is the endolymph, by the inertia of which, as the hair cells of the *crista* are dragged through it, an apparent current is produced in a direction opposite to that of the movement. In the vertical canals, the principal function is called forth by the flow of endolymph from the vestibule through the ampulla toward the canal, and the subordinate function, by the flow in the opposite direction; in the external canals, the direction of the flow is the reverse. The fact of a double function necessitates the hypothesis of the presence in each *crista* of two functionally different kinds of nerve ending. Mechanical stimulation of the whole ampulla produces movements of eyes and fins, that indicate the activity of the principal function.

The loss of a single canal does not greatly interfere with the animal's dynamical equilibrium; his compensations for rotations in planes mediated by the canal may be modified. The added loss of the functional opposite intensifies the modification. The loss of a functional pair of canals displaces eyes and fins, may apparently remove

the compensating power for the rotations normally mediated by the lost organs, and may introduce such rotations as "forced" movements. Such displacement of eyes and fins and such forced movements are caused by the abnormal presence of sensations of movement, normally mediated by the functionally opposite pair. The added loss of this latter pair restores the eyes and fins to their normal condition, and puts an end entirely to the compensating power belonging to the lost canals, while forced movements toward either pair of canals are possible. The loss of the three canals of one side displaces eyes and fins, greatly weakens compensation, and may introduce forced rolling or circus movements toward that side; with the loss of the six canals, the compensating power for all planes is gone, forced movements may occur, the sense of dynamical (rotational) equilibrium is wholly wanting.

The sense-organs of statical equilibrium are the vestibular portions of the ear with the *maculæ acusticæ* and the otoliths—at least those of the *recessus utriculi* and *sacculus*. The normal stimulating agent is the otolith pressing upon the hair cells of the *macula*. Mechanical stimulation may call forth all movements of eyes and fins that may be obtained through the ampullæ. The removal of otoliths from one ear interferes to a considerable extent with statical equilibrium, evidenced by abnormal positions of eyes and fins and trunk; removal of otoliths from both ears practically abolishes the sense of statical equilibrium, while rotational power is still intact.

Cutting one acoustic is equivalent, as regards equilibrium, to cutting all ampullar branches and removing the otoliths upon the same side; cutting both nerves practically abolishes the senses of both statical and dynamical equilibrium.

The leading conceptions of the present investigation may be tabulated as follows:

Equilibrium Functions of the Ear.

I. Dynamical Functions.
   A. Normal: Sensations of rotational movement, accompanying corresponding compensating movements of eyes, fins and trunk; varying according to the nerve stimulated.
   B. Pathological: Abnormal sensations leading to abnormal positions of eyes, fins and trunk, and to forced movements; varying according to the nerve cut.

(Localization of dynamical functions in semicircular canals; stimulation during body movement.)

II. Statical Functions.

A. Normal: Sensations of position of body in space accompanying corresponding positions of eyes and fins; varying according to the nerve stimulated (?).

B. Pathological: Abnormal sensations causing lack of orientation and abnormal positions of eyes, fins and trunk; varying according to the nerve thrown out of function (?).

(Localization of statical functions in otolithic parts; stimulation continual.)

VIII. Bibliography.

For an exhaustive list of the publications dealing with the equilibrium functions of the internal ear, the reader is referred to Ewald, "Physiologische Untersuchungen über das Endorgan des Nervus Octavus," Wiesbaden, 1892. The appended references are to articles specially referred to in the accompanying text.

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Reprinted from the New York Medical Journal for March 10, 1894.

NOTES UPON SOME KYMOGRAPHIC TRACINGS OF TREMOR.

By FREDERICK PETERSON, M. D.,

CHIEF OF CLINIC, NERVOUS DEPARTMENT, VANDERBILT CLINIC, COLLEGE OF PHYSICIANS AND SURGEONS, NEW YORK.

In a paper entitled A Contribution to the Study of Muscular Tremor, read before the American Neurological Asso-

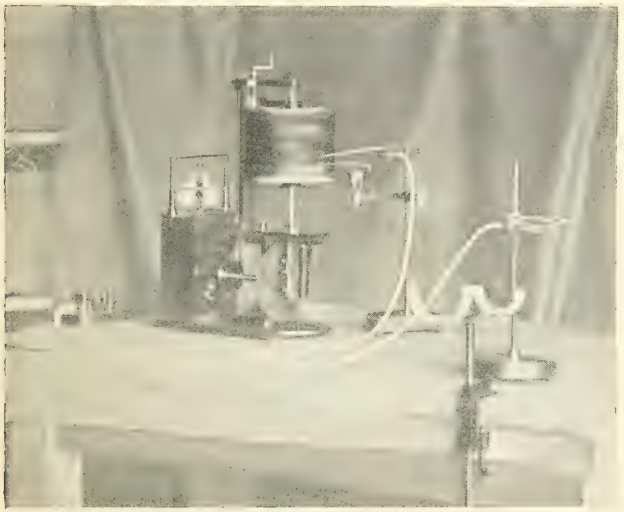

FIG. 1.—Apparatus used for taking tremor tracings. Ludwig's kymograph with electric connection for seconds. Two Marey's tambours joined together by a rubber tube. Arm-rest screwed to table.

ciation in 1888,* I gave the details of observations upon the tremors of paralysis agitans, Graves's disease, multiple

* *Jour. of Nerv. and Ment. Disease*, February, 1889.

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FIG. 2.—Tremor of paralysis agitans, showing dicrotism. Rapid revolution of drum of kymograph.

sclerosis, hysteria, neurasthenia, and alcoholism, the tracings of which were taken with the Edwards sphygmograph. The rate of these tremors, as determined in this way, I made out as follows:

	To the second.
Paralysis agitans	3·7 to 5·6
Morbus Basedowii	8·7 to 12
Multiple sclerosis	5·4
Hysterical tremor	7·7
Neurasthenic tremor	7·4
Delirium tremens	5.6
Chronic alcoholism	8·5 to 11·2
Ankle clonus in primary lateral sclerosis	6

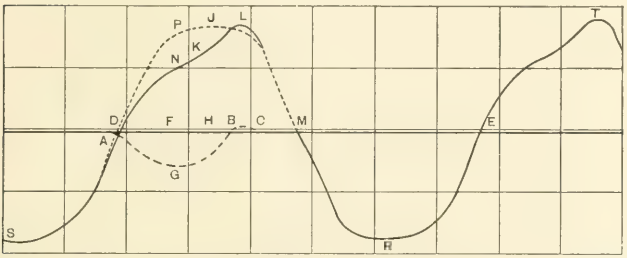


FIG. 3.—Geometrical analysis of paralysis agitans wavelet taken from upper right hand corner of Fig. 2.

While the sphygmograph does in reality serve sufficiently well for ordinary clinical purposes in the registration of these tremors, it is not satisfactory from a scientific point of view, because it is not exact in the determination of the rate. Take, for instance, the following table from my chapter on Paralysis Agitans in Starr's *Familiar Forms of Nervous Disease:*

Author.	Publication.	Rate to the second.
Marie	*Contrib. à l'étude*, etc.	5
Charcot	*Mal. du système nerv.*	4–5
Ewald	*Berl. klin. Woch.*, 1883, No. 32	5
Grashey	*Arch. für Psych.*, 1885	4·14–5·34
Huber	Virchow's *Arch.*, vol. cviii, p. 45	3·43–5·57
Gowers	*Dis. of the Nerv. Syst.*, 1888, p. 1001	4·8–7
Wolfenden and Williams	*Brit. Med. Jour.*, May 19, 1888	5·1
Peterson	*Jour. of Nerv. and Ment. Dis.*, Feb., 1889.	3·7–5·6

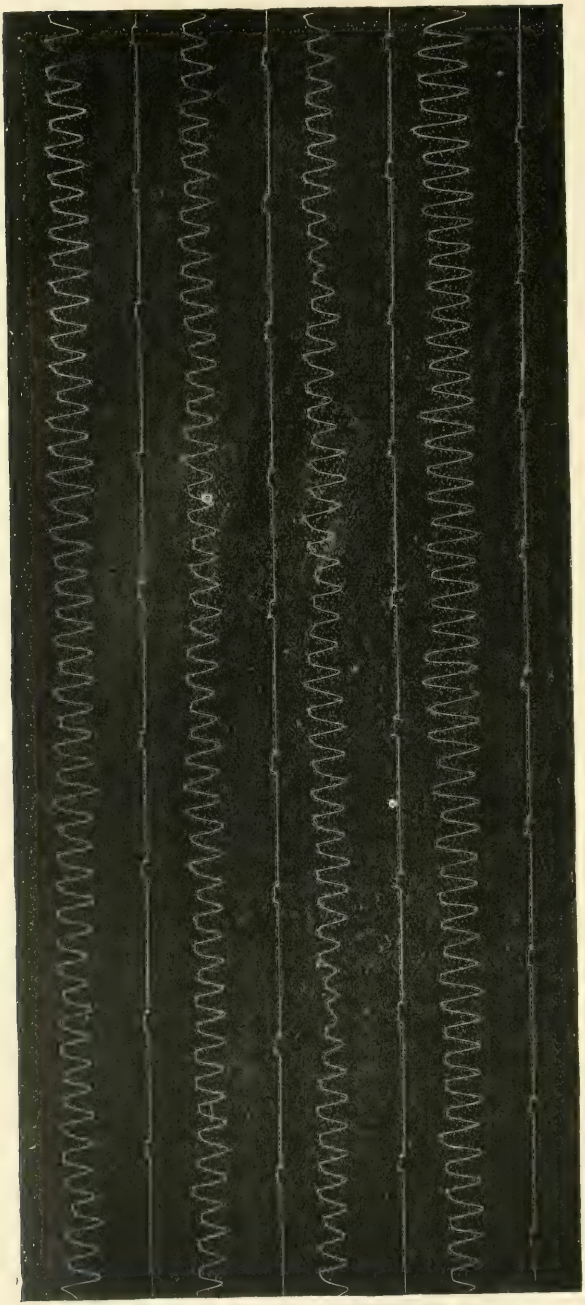


FIG. 4.—Tremor of paralysis agitans. Slower revolution of drum.

Most of these authors used the antiquated Marey sphygmograph, which is much more inexact than that of Edwards, employed by myself. From this table, giving the rate of tremor in paralysis agitans as noted by divers authors, it will be seen that there is great variation in the figures. Wolfenden and Williams made use of a kymograph, and approached very near to what I conceive to be the actual rate of this tremor to the second.

Quite lately Dana (*Medical News*, Dec. 17, 1892) has employed the Dudgeon sphygmograph for the same purpose, making the rate of tremor in paralysis agitans from 3 to 6·1 per second. This great variation I believe to be due rather to the instruments made use of than to differences in the rate of the tremor itself.

In Fig. 1 is shown the Ludwig kymograph, with its electric connection for seconds, and the two Marey tambours joined by a rubber tube, and also the rest for the arm while the tremor is being taken. The advantages of this apparatus are the greater accuracy of the time rates and the ability to modify the revolution of the drum so as to magnify the tremor waves. Rapid revolution of the drum magnifies the waves so that each wave may be carefully studied in all its details, and dicrotism becomes markedly visible. The apparatus was set up in the physiological laboratory of the College of Physicians and Surgeons, and patients were taken from the Vanderbilt Clinic for purposes of study. I am indebted to Professor John G. Curtis for placing it at my disposal.

In Fig. 2, on page 2, we have four tracings taken from a case of paralysis agitans, the drum being rapidly revolved so as to magnify the tremor waves. The movements represented are of the flexors and extensors of the wrist. The tendency to dicrotism is very pronounced, and the rate per second is seen to be exactly 5. Just beneath each tremor wave is the line indicating the seconds. Mr. A. E. Kennelly, of the Edison Laboratory, kindly volunteered to make a geometrical analysis of some of these waves, with a view to possibly determining some interesting features of diagnostic value. Thus, if the waves were constantly of the same character, we could always attribute a certain outline to a certain cause, and thus impulses and

FIG. 5.—Tremor of paralysis agitans. Still slower revolution of drum.

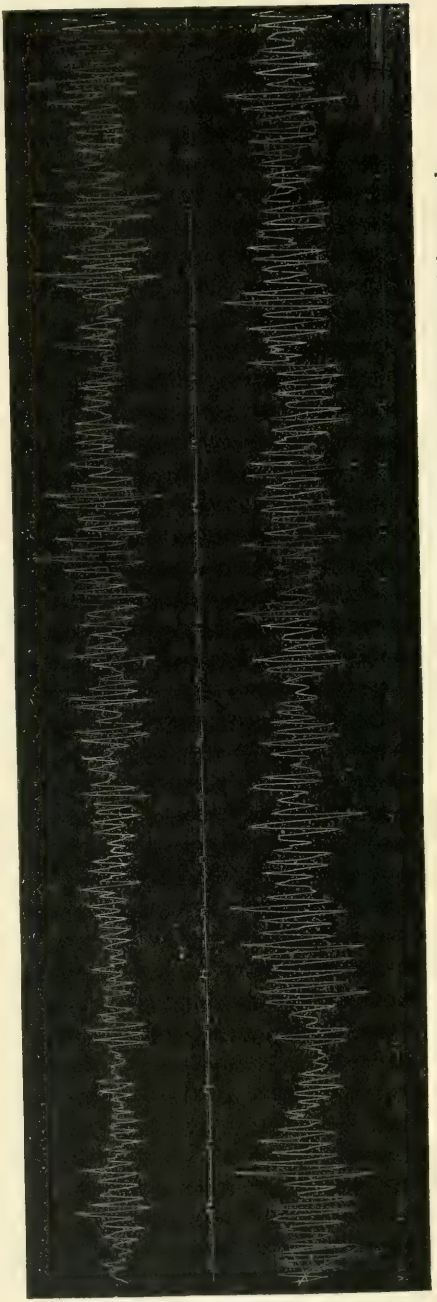


FIG. 6.—Tremor of paralysis agitans. Slow revolution of drum. Singular grouping of series of waves, each four seconds.

activities not visible in the aspect of the waves as a whole might be discovered. With a series of waves, such as liquid waves through elastic tubes (the pulse), this careful geometrical analysis would undoubtedly prove of great

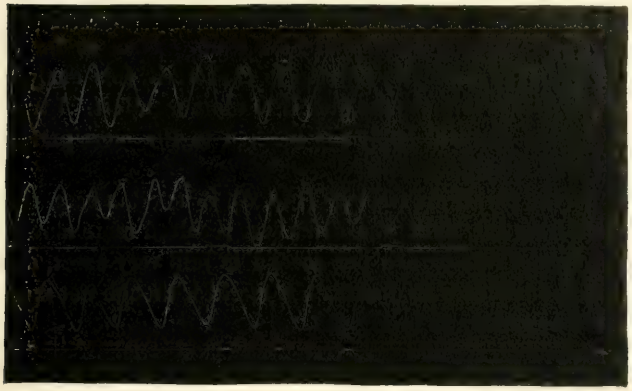


FIG. 7.—Tremor of paralysis agitans. Rapid revolution of drum.

value, for here the current velocity, the elasticity, and the resulting wave train are almost invariable. But where, as in the tremor waves above given, variation is considerable, such analysis is exceedingly difficult and must be carried

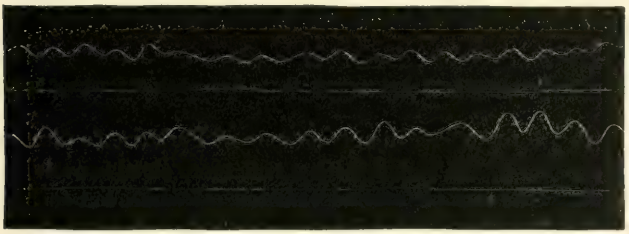


FIG. 8.—Tremor of alcoholism. Rapid revolution of drum.

through the whole series, a laborious task and enough to dishearten one who undertakes it. However, I present the results of Mr. Kennelly's work for what it may be worth. He carefully transferred by micrometer measurements a pair of waves from the upper train of Fig. 2 to large scale paper. The curve (Fig. 3) S I N K L M R E T can in its first half wave length be analyzed into components, one of which

is the second semi-wave, M R E, inverted, and the other a smaller opposite wave in dotted line, A G B. The opposite wave has two thirds of the main wave length and one third of the main wave amplitude, so that (neglecting as a possible discrepancy the wavelet B C unaccounted for) there is a main train of waves, with a semi-train superimposed upon it, making a compound wave-train. Thus, as far as the tremor of paralysis agitans is concerned, this analysis merely serves to make the dicrotism more manifest. I trust that some one will apply the method to the more perfect waves of sphygmograms.

In the preceding tracings (Fig. 4), in another case, also taken from the wrist, the drum was revolved more slowly. The tremor rate of five per second is still very exact, and even the tendency to dicrotism is marked, though not magnified so greatly as in Fig. 2.

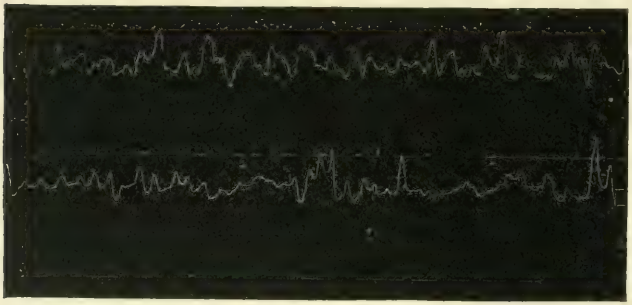


Fig. 9.—Tremor of hemiplegic polymyoclonus from whole of paralyzed hand

Fig. 5 represents in another case of Parkinson's disease the tremor of the thumb with a still more slowly revolving drum. The rate per second remains the same, but such a tracing is no improvement upon one obtained from a sphygmograph. The evenness of the tremor of paralysis agitans is the only characteristic feature.

Fig. 6 is a tracing also from the thumb, in another case where the tremor was very marked and the excursions wide. The revolutions of the drum were at the same slow rate as in the last. A remarkable feature of this tracing is a manifest tendency to a grouping of the waves about every four seconds, as if the innervation impulses were invigorated every few seconds. I could not deter-

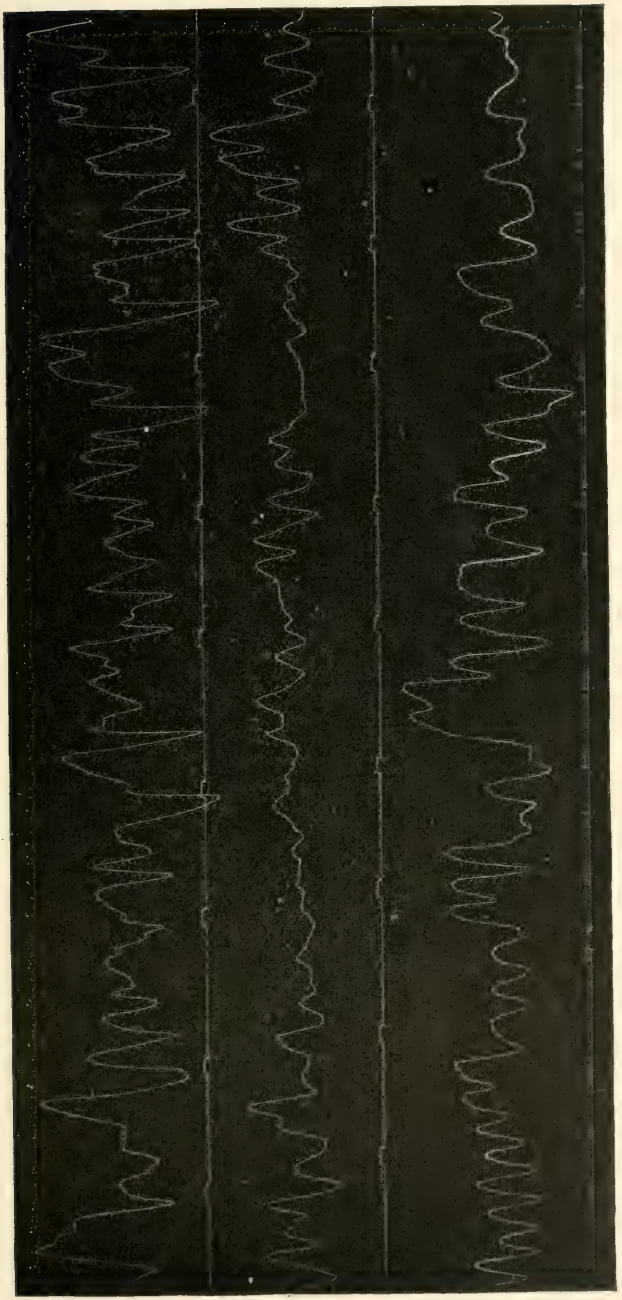


FIG. 10.—Tremor of methemiplegic polymyoclonus. Taken from the thumb only.

mine whether this was due to some respiratory influence or to some unknown factor (such as nutritional rhythm in the cortical cells?). This is certainly worthy of further study. In another group of tracings, unfortunately lost, this peculiarity was much more pronounced.

Fig. 7 is a series of ring finger tracings of the tremor of paralysis agitans with a rapidly revolving drum. While the rate of five per second is very apparent here, the greatness of the excursion prevents the development of the dicrotism, which was so marked in the cases where the wrist muscles were investigated.

In Fig. 8 we have the fine tremor of alcoholism greatly magnified by swift revolution of the drum. From a careful study of this tremor in a long series of many tracings I find the rate to be ten to the second. The above tracings show merely one or two seconds out of five or six on the same piece of paper. The uniformity of the tremor is also marked. Some tremors of Graves's disease and of general paresis were so similar in character and rate (ten to the second) that they are not reproduced.

Some time ago I called attention to a variety of post-hemiplegic movements (*Trans. N. Y. Neurolog. Soc.*, Dec. 6, 1892) following infantile spastic hemiplegia, to which I gave the name methemiplegic polymyoclonus. It is a rare phenomena, for out of over two hundred and fifty cases of infantile cerebral palsies that have come under my observation I have seen but two with this form of morbid movement. It consists of rapid and not synchronous clonic spasms in the muscles of the limbs affected. The excursions of the separate muscles are about equal to those of paralysis agitans and the rate is five to the second. Indeed, if the muscles moved synchronously, the condition would be exactly analogous to paralysis agitans. The tremor is constant, and only ceases during sleep. It would be improper to call it either athetoid or choreiform, and hence my selection of a new designation. The character of this movement is indicated by Fig. 9. Here the whole hand clasped a bulb connected with the tube leading to Marey's tambour and the delineator. The inco-ordinated and rapid movement is shown in the irregularity of the wave train. The drum revolved slowly in fifty-three seconds, and only

about a third of the completed tracings is shown. The movement in the thumb alone is shown in the three tracings of Fig. 10.

In closing I will merely say that compared with the kymograph the sphygmograph is of course crude and uncertain in the registration of these various tremors. Most tremors can, I think, be placed in two categories—one a fine and rapid tremor at the rate of ten to the second, corresponding to the normal innervation rhythm as determined by Horsley and Schafer, and one a slow tremor wherein the normal innervation wavelets are fused into groups of two, giving an apparent rate of five to the second.

Reprinted from *The American Naturalist*. Vol. XXVIII, May and June, 1894.

THE SCOPE OF MODERN PHYSIOLOGY.[1]

By Frederic S. Lee.

A review of the present aspect and tendency of a rapidly growing science in the light of its history may not be without profit. It may help to clearer vision and more exact orientation: and it may direct and stimulate investigators. These thoughts, together with the prevalence of an apparent misconception regarding the true aim and scope of Physiology, have led to the following paper.

To one who is acquainted with modern biology, it will seem unnecessary to repeat that physiology is the science of function or action: that it is to be contrasted with morphology, the science of form or structure: that these two form the grand divisions of the science of living things, or biology: that, just as there is an animal and a vegetable biology, so there is an animal physiology and a vegetable physiology: that, further, every species has its physiology: that every portion of living matter, be it organism, organ, tissue, cell, or simplest group of molecules deserving the name protoplasm, Weismann's biophor, has its physiology: that, for whatever functions or acts, there must be possible a science of function or action. All this seems self-evident and trite to the biologist. By the non-biologist its truth is being overlooked constantly. To him, forgetting that botany and zoology exist, the term physiology means merely *human* physiology, a most narrow significance and one that is productive of evil results. Undoubtedly the animal physiologists themselves have been responsible, unintentionaly and unwittingly, for this common and radically false notion of the relatively narrow field of their science. In their zeal to penetrate the mysteries of that most wonderful and most interesting of all protoplasmic structures, the human body, and in their desire to perfect a strong foundation for the science and art of medicine, it was to be expected that their investigations should have an "anthropocentric" bias

[1] Read before the Section of Biology of the New York Academy of Sciences, November 20, 1893.

and that physiology and medicine should be born and grow old together. Let a union so intimate be once established, let centuries of tradition surround and strengthen it and the separation is not an easy process. With special reference to this question and at the risk of treading upon well-known historic ground, what has been in brief the history of animal physiology?

It is convenient to divide it with Preyer into five periods: the first four ending approximately with the dates 350 B. C., 160 A. D., 1628, and 1837, respectively, the fifth extending to the present time. The last four periods are characterized by one or more prominent investigators, the second by Aristotle, the third by Galen, the fourth by Harvey and Haller, the fifth by Johannes Müller.

The beginnings of animal physiology were contemporaneous with the speculations of the earliest natural philosophers and the labors of the earliest physicians. In Egypt, in China, in India, in Greece, the origins of the science are necessarily indefinite and, with the help of occasional fragments of historical fact, must be left to our imagination. The inclination toward self-study is an innate human characteristic and the more obvious facts of man's bodily functions could scarcely have failed of notice. Something was doubtless learned from the bodies of men killed or wounded in battle, and from the slaughter of animals for food. More precise observations were made upon sacrificial animals for purposes of divination. But facts thus obtained were necessarily isolated, and abundant speculation was the distinguishing characteristic of the whole period. From its shadowy beginnings down to the death of Hippocrates and Plato, the theories that were held regarding the origin and nature of life, unsupported, as they were, by observation and experiment, could not establish a science of vital action. Even Hippocrates himself, skillful as he was in the treatment of diseases, was no physiologist.

At the beginning of the second period was Aristotle, the first systematic observer of natural phenomena. His knowledge of physiological fact was derived, as is well known, in greatest part from his own observations on man, the lower animals, and plants; and to a large extent it forms the basis of all subsequent development of the science. His pupil, Theophrastus, founded the science of vegetable physiology. Contemporaneous with Theophrastus was the development of

the great school of medicine at Alexandria, and here, under Herophilus and Erasistratus, animal physiology, along with anatomy and pathology, as a part of medicine undoubtedly made great progress. The extent of that progress can be inferred only imperfectly from later writers. The loss of the Alexandrian records is most lamentable. Aristotle had dissected animals; the Alexandrians dissected the human body and, more important for our science if true, it is possible that they performed experiments on animals. The facts made known by Aristotle were added to; physiological material accumulated. Thus, while the first period had been speculative, the second was descriptive. But not yet was there a *science* of function.

Then came Galen, the great physician, investigator, and writer and it was he who organized the mass of knowledge that through the centuries had been growing. From Galen's time animal physiology has had a recognized position as a branch of natural science. A modern writer[2] says of him: "In the midst of contending factions he alone and for the first time shaped physiology into an independent science. He established physiology as the doctrine of the use of organs; he experimented upon animals . . . ; and he suggested questions which he answered by the aid of such experiments. In opposition to all his predecessors and contemporaries, he maintained physiology to be the foundation of medicine. Further, he, first of all and so far as it was possible at his time, described and explained the functions methodically and completely. Upon the one side he sought to refer vital phenomena to natural causes, and upon the other he lauded their purposeful character, with expressions of admiration for the wisdom of the Creator, while their fitness aided him in explaining them. . . . The fact that the Galenic physiology, wherever it was known, prevailed for fifteen hundred years is due to its two-sided development. For physicians accepted it because of its materialism, and the clergy because of its teleology. Since Galen was an extraordinary sagacious thinker, an uncommonly learned man, an industrious, systematic, truth-loving worker and skillful physician, never neglecting practice for research nor research for practice, of all the medical fraternity he seemed best fitted to lay the corner-stone of physiology as a science in itself. And it testifies to his genius

[2] Preyer, *Allgemeine Physiologie.*

that, in the whole thousand years following him, Galen's physiological system, constructed through his originality and the power of his logic, endured as law, seriously opposed by no one. The history of no science can show the like. Faith in the authority of Galen's name finds its equal only in the history of religions." It is to Galen's influence, doubtless, more than to that of any other, that the intimate union of physiology and medicine, continuing even to the present day, is due. And to him likewise we must ascribe the present prevailing idea, already spoken of, of the essentially human character of the science. Galen's physiology was in essence a human physiology; and the new science fully born became the handmaid of medicine. Galen's authority was supreme until the age of the Renaissance, and throughout the long mediaeval period animal physiology was at a standstill. Toward its close the Italian universities were established and men began to think for themselves, to read nature in addition to the books, and gradually to learn that nature and Galen did not always agree. The elaborate and ill-founded hypotheses of the spirits, the elements, the qualities, and the humours did not accord with the progressive, investigating spirit of the Renaissance, and rebellion against the master gradually grew in strength. Paracelsus burned in public at Basel the works of Galen. More destructive than fire were the anatomical investigations of Vesalius and Fallopius. And in physiology Colombo and Caesalpinus prepared the way for the most important single discovery of the time. This event, which more than all else demonstrated the ineffectiveness of pure speculation and the need of a rational method of observation and experiment, was none other than the discovery of the circulation of the blood.

With the announcement of this to the world in 1628, what we have called the fourth period of physiological history begins. Harvey's book, "*De Motu Cordis*," is a model record of an ideal scientific investigation. The accumulation of an abundance of the essential facts, obtained by a most careful and systematic study of nature, the clear understanding of their logical positions and their mutual relations, and then, unhampered by scholastic systems and *a priori* considerations, but guided only by a regard for truth, the orderly arrangement of the accumulated material into the one possible rational system—such was Harvey's method. The result was

incontrovertible. The full title of Harvey's work is "*Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus*," but Harvey himself, being a physician, and his contemporaries and followers naturally enough considered more especially the human bearing of the established facts. For two hundred years after, discovery followed discovery, and the permanent foundations of the various subdivisions of physiology were laid—circulation, respiration, animal heat, the functions of the central nervous system and of the peripheral nerves, movement, animal electricity, reproduction, optics and acoustics. Haller's well-known contribution was that of the independent irritability of muscle. Of perhaps as much value were his complete knowledge of physiological literature and his activity in writing. In 1747 he published a text-book, the "*Primae Lineae Physiologiae*," and in 1757 the large and complete "*Elementa Physiologiae Corporis Humani*." These books were widely circulated and the entity of the science was forever established. The title of Haller's larger work, "Elements of the Physiology of the Human Body," indicates that its "anthropocentric" character was stamped firmly upon it. By its independent growth, its subordination to medicine was, however, already weakened.

To enumerate its advances during the past fifty-six years, the fifth period, would be a task of great proportions. The man to whom it is customary to give the credit for having outlined the path that was to be followed during his lifetime and for the generation that has elapsed since his death, the teacher, either personally or by his writings, of the veterans, Ludwig, du Bois Reymond, Brücke and Helmholtz, was Johannes Müller. Müller's name will at once suggest the one important principle that he formulated, that of specific nerve energies, but his writings and discoveries cover a wide field. His extraordinary knowledge, energy, enthusiasm and stimulating power were all-important during a period so rich with biological achievements. It is perhaps a fair question, whether Magendie, with his marvellous activity as an experimentalist, may not dispute with Müller the honor of having given to the physiology of the past fifty years its characteristic trend. Certain it is that he fathered the science in France (Claude Bernard was his pupil); that his writings were read much across the Rhine; and that the labors of the Germans have been, like his, the collecting of facts rather

than the constructing of systems. Within this half-century the establishing of the two great doctrines of physics, the mechanical theory of heat and its greater corollary, the conservation of energy, were of indispensable aid to the development of physiology. The idea of vital force had taken on many forms and the controlling principle of life had played its part under many titles. But, when it was shown that in the inorganic world the various kinds of energy are mutually interchangeable, physiologists, long hampered by and impatient under the old ideas, eagerly seized upon the new, in fact, aided not a little in their discovery, and proved that they applied to living things as well as to the not-living—and, with this, freedom from unscientific speculation was won: the animal is a machine in a sense more complete than the Cartesian one. On the purely physiological side of biology, this is undoubtedly the greatest achievement of the present century. Until the substance of the plant and the animal body could be regarded as subject to the same laws that controlled all other matter, much must have remained mysterious and inexplicable and physiology could not be reckoned as all in all a natural science. Psychology has always been hampered by the speculations of the system-loving metaphysicians. More actual fact and less conjecture are essential to the scientific method: and the scientific method is the method of progress. Following this freedom from the doctrine of vital force, physiology has developed actively along two main lines, the chemical and the physical including the mechanical, and is now often defined as the chemistry and the physics of living matter. An astonishing number of discoveries have been made, and the outlines that were sketched by Galen and Harvey and Haller and Müller and Magendie have been filled in with remarkable rapidity and completeness.

Let us consider for a moment the prominent characteristics of the work of this period. In the first place, Vertebrates have received more attention and have been the subject of more systematic investigation than Invertebrates. And among the Vertebrates, with the exception of the indispensable frog, which, however, is rarely regarded as a finality in research, the Mammals, being nearest to man have been most studied. Second, the number of forms used is very small: it is probably safe to say that the genera employed in four-fifths of the researches could be counted easily upon the fingers of the two

hands. Third, adult animals have been used almost exclusively. Fourth, the study of organs has prevailed, *i. e.*, the investigator has endeavored to discover the chemical, physical and mechanical laws by which the heart, the lungs, the glands, the muscles and the brain perform their respective tasks. These characteristics are the natural outcome of the birth and growth of the science. They indicate that, although the results accomplished are widespread and of the greatest value, there are left almost untouched still wider fields. The achievement of so much, however, along the lines of the past is stimulating to the student of to-day, for it has made possible the more rapid development of the science in the new directions in which it is now tending. To these we shall return shortly.

I think that the historian of the present period will not fail to be struck by the comparative paucity of hypothesis in physiological research, especially when our science is contrasted with the other great division of biology. It is as if men had been nauseated by the vitalistic doctrines and other wild guesses of the past and had resolved hereafter to hold strictly to the Baconian method. At the risk of being misunderstood and criticised, I cannot help feeling that this is to be deplored. The method of all physical science is truly observation and experiment: facts must be discovered and grouped and the laws formulated therefrom. But, in the search after facts, the inestimable value of hypothesis—of speculation, if you will—cannot be denied. It directs the searcher along a definite path and gives for the time being an encouraging and stimulating coherence to his results. If later his speculation becomes verified, well: if it proves false, its use is not to be deprecated, for it has served its purpose as an aid to discovery. The facts still remain, science is by so much the gainer, and with a new interpretation and a new hypothesis nearer the truth further advance will be made. The trouble is to keep the speculation within rational bounds and to know when to give it up. To employ it too sparingly is to retard scientific progress, and it seems to me that just here the animal physiologists of the present period are open to criticism.

Further, it is to be noted that until far into this period throughout the Continental, the English, and most of the American universities physiology and anatomy have together

formed one department. At Bonn from 1826 to 1833, and at Berlin from 1833 until his death in 1858, Müller occupied such a common chair. Helmholtz held a similar position in Bonn from 1855 until 1858. Now, everywhere, animal physiology presupposes anatomy, and each science has its own field and its own methods. Further still, physiology usually occupied a place in the Medical faculty. This also is the result of its historical development. As I have shown, it is to the medical fraternity, more than to any other one class, that it owes its great progress in the past. But a glance at the literature of the present period will show that, largely through the efforts of its medical promoters, it has widely overstepped its early medical boundaries. It has long since ceased to be a purely medical and anthropological science; it has become a biological science. Human physiology, like human anatomy, will necessarily always form one of the foundation stones of a medical training, and perhaps the most important one. But human physiology is but one branch of a science as broad as are the domains of protoplasm. Man's body is a machine, but it is a machine that has had a history. It is an achievement to learn to know the mechanical, chemical, and physical laws of this most complex of vital mechanisms. But the task of the physiologist does not end here—I should say it does not begin here. To know the action of the mechanism without its history is not only short-sighted, it is impossible. This is being recognized and a school of general and comparative physiologists is arising. During the present period, then, besides its great advance along the older lines, our science has begun a development along broader biological paths. It has won a place as an independent, pure natural science. More and more are its claims to admission to Pure Science and Philosophical faculties being recognized. It should be placed and will be placed by the side of chemistry, physics, and the morphological division of biology. I do not think it an exaggerated statement, that the tendency of biological thought at present is toward extraordinary activity along physiological lines.

Three achievements of the present period have shown investigators how broad their science really is. First, the establishing of protoplasm as the physical basis of life, and of its substantial identity in plants and animals by Dujardin, von Mohl, and Max Schultze, showed that the really fundamental

problems of life and action had heretofore not been grasped; that the essential laws of protoplasmic activity apply to the whole organic world; and hence that any physiology which confines itself rigidly to either plants or animals to the exclusion of the other is a one-sided science. Second, the cell-theory of Schleiden and Schwann demonstrated that sooner or later many functions must be traced back to the cell, and that a cellular physiology is the key to a large proportion of the problems arising in the biological world. Third, the work of Darwin, based, as it was, upon physiological principles, showed that the action of the environment upon the individual and upon the species, as well as the action of the organism upon the environment, was an almost unworked field of the richest promise; that all physiology, in order to be complete, must be comparative; that there is an ontogenetic and a phylogenetic evolution of function; and that the physiological laws of heredity were yet to be discovered.

Let us examine these ideas briefly. The necessity of understanding the physiology of undifferentiated protoplasm is obvious, for there we find function in its simplest and most generic form. The phenomena of projection and retraction of pseudopodia in the Amoeba are doubtless the key to the complex processes of contraction and relaxation of striped muscular tissue. It is not at all improbable that the action of light upon the retina is a specialized derivative of the heliotropic phenomena of the simplest plants and animals. Four years ago, the well-known Oxford physiologist, Burdon Sanderson, wrote concerning the nature of physiological inquiry, "The work of investigating the special functions, which, during the last two decades, has yielded such splendid results, is still proceeding, and every year new ground is being broken and new and fruitful lines of experimental inquiry are being opened up; but the further the physiologist advances in this work of analysis and differentiation, the more frequently does he find his attention arrested by deeper questions relating to the essential endowments of living matter, of which even the most highly differentiated functions of the animal or the plant organism are the outcome." Again, "No one who is awake to tendencies of thought and work in physiology can fail to have observed that the best minds are directed with more concentration than ever before to those questions which relate to the elementary endowments of living matter, and that if they are

still held in the background, it is rather because of the extreme difficulty of approaching them than from any want of appreciation of their importance. . . . If we really understood them, they would furnish a key, not only to the phenomena of nutrition and growth, but even to those of reproduction and development. . . . It is in the direction of elementary physiology, which means nothing more than the study of the endowments of living material, that the advance of the next twenty years will be made."

Regarding the need of a cellular physiology, it is only necessary to review our knowledge of any one of the complicated organs to perceive that aside from the principles, often chiefly mechanical, involved in the work of the organ as a whole, the essence of its activity lies in the activity of its component cells. The work of the muscle, *e. g.*, is the sum of the activities of its constituent physiologically similar fibres. A single gland cell illustrates the principles of secretion as well as, or even better than, a thousand grouped together into a compact gland. The complexity of brain operations is due to the complexity of brain structure, but the active agents are the comparatively simple nerve-cells. Huxley sets forth as the first three of the five chief ends of modern physiology: "Firstly, the ascertainment of the facts and conditions of cell-life in general. Secondly, in composite organisms, the analysis of the functions of organs into those of the cells of which they are composed. Thirdly, the explication of the processes by which this local cell-life is directly, or indirectly, controlled and brought into relation with the life of the rest of the cells which compose the organism." Now that the structure of protoplasm is fast becoming disentangled, a rational cell-physiology will be possible. In urging the need of investigating cell-function, I do not mean to imply that the cell is necessarily the ultimate unit, and that the organism is to be regarded as substantially a colony of physiologically independent cells. Much of the recent cytological work indicates that ere long the cell may be deposed from its hierarchical position.[3] Cellular interactions are to form an increasingly prominent place in the researches of cell-physiologists. But, whether or not we grant with many that the cell is of secondary significance, we must allow that, in many respects at least, it may be regarded as a physiological unit: and from this standpoint it demands investigation.

[3] Cf. Whitman, *Journal of Morphology*, VIII, No. 3, August, 1893.

In these days of comparative science, it seems superfluous to urge the necessity of a comparative physiology. No one, who thinks seriously of the matter, will doubt that along with the morphological distinctions between different species, genera, orders, or classes, and even in cases where gross morphological distinctions are not apparent, there must be physiological differences. Beyond the obvious facts of simple observation, these are almost wholly uninvestigated. de Varigny, in his suggestive little book on Experimental Evolution, has collected a number of the known facts. In a garden in the south of France, were growing, side by side, a number of plants of the same species. There appeared to be no morphological differences between them, but some were indigenous to the soil in which they were growing, while others had been imported from the Canary Islands. When they were attacked by frost, all the Canary Island forms perished, while the French forms were untouched. There was evidently some obscure physiological difference between them. The two common European species of frogs, *Rana temporaria* and *Rana esculenta*, behave very differently toward certain drugs, as Schmiedeberg, Monnier, Vulpian, Harnack and Meyer, and others have shown. In *R. tempororia*, caffeine causes a decrease in excitability, in *R. esculenta* an increase; in *R. temporaria* pilocarpine causes paralysis, in *R. esculenta* tetanus. The venom of one snake is harmless for its own species, but poisonous for others. The spinal cord of the fish is differently endowed from that of the frog, though the differences have never been properly investigated. The muscle of the Insect is far removed functionally from that of the Crustacean, though how far remains to be discovered. I do not overlook the fact that already much excellent work upon the physiology of the Invertebrates and lower Vertebrates has been done, but too often such work has not been *comparative*. Fitness for the object of the research is the usual determinant of choice—and hence the frog has taught us most of our physiology of muscle. Sooner or later this must all be changed, the functional differences must be made known, and the exact position of each plant, each Invertebrate, and each Vertebrate, in the physiological series, together with the exact position of his organs and tissues and cells must be understood. For we must recognize the fact that function in any one species has *come to be*—an evolution of function is as much a reality as an evolution of form. The

adult body and its organs, tissues and cells are the functional derivatives of the germ-cells—in the growth of the individual there has been a physiological ontogeny. So in the growth of the species there has been a progressive or retrogressive development of function; and one of the most attractive fields for our future work will be the tracing out of the phylogeny of function, now a practically unknown subject.[4] The difficulty of such an undertaking is great, for the rich palaeontological series is beyond the reach of the experimentalist. Yet this should be no bar to the systematic investigation of existing forms. Such a phylogeny will vary with each functional part (organ, tissue or cell); *e. g.*, if, in one genus, certain brain functions and certain secretory functions are always found, the presence of the same brain functions in another genus does not necessarily indicate the presence of the same secretory functions. Nor will the line of functional descent of a part necessarily coincide with the line of morphological descent of the organism. A natural system of classification is based and, justly so, on morphological considerations. In thus tracing out the genetic relationships of function, lie the attractiveness and the utility of the comparative method in physiology. And I venture to assert that, if all investigators would bear in mind the fact of an evolution of function, surprising advances would result in our knowledge of the working of adult organs.

What is it that makes an individual physiologically what he is? There are two agents—heredity and the environment. As to heredity, the active discussion now going on around Weismann as a center, serves to show what a vast amount we do not know, on both the morphological and the physiological sides, as regards the general phenomena of heredity and the nature and behaviour of the hereditary substance. No one recognizes this more fully than Weismann himself. He confesses that his own theory is far from complete; that its importance consists primarily in its suggestiveness; that the real solution of the problem lies in the future, and that facts are greatly needed. In this connection I may refer to the value of the work of Nussbaum, Gruber, Balbiani, Hofer, Korschelt, Verworn and others on the physiological relations of the nucleus and cytoplasm.

The mutual relations of the environment and the individual are almost as unknown as when Darwin first demonstrated

[4] Cf. Dohrn, *Das Princip des Functionswechsels.*

their importance. In a few special lines they have been investigated. In his earthworm studies Darwin himself set an eminent example. The fact of the modification of the virulence of pathogenic bacteria by their treatment during growth is well known. Interesting results have been obtained regarding the action of salt-water on fresh-water animals, and *vice versa*: the action of salts on starch production in plants; the effect of depriving animals of apparently important salts, *e. g.*, fowls of carbonate of lime, and crabs of calcium chloride. Maupas's well-known studies on the influence of temperature on the determination of sex may be mentioned here, as well as those of Yung, Mrs. Treat, and others on the influence of foods. If an altered environment is capable of altering function—and we know this to be a fact—and if the altered function reacts upon structure—which is equally undoubted—then we find in these premises sufficient justification for searching after the facts concerning the nature and extent of environmental influence. The value of such researches lies not so much in the isolated results themselves, as in the fact that such results, when sufficiently numerous, will lead us directly not only to a better understanding of the internal physiology of organisms, but, what is of more general interest, to an understanding of the causes of variation, and thus to a better comprehension of the relations of species to one another. Too much cannot be said upon this phase of our subject. Whether the direct action of the environment is to be considered as a factor in organic evolution or not, the causes of variation must be investigated *experimentally*, and the physiological side of the work must not be neglected. Semper says, "Although the morphological section of animal biology[5] teaches with much probability that this species or that organ has undergone this or that course of modification in the animal series, and that in the process of modification it has passed through a whole series of various forms, still it is only physiological research that can elucidate the necessity for their existence by revealing their causative conditions."

One word regarding the relations of physiology and morphology. In the broad way in which I have outlined the former science, it may be charged that I have trespassed upon the morphological preserve. I do not deny the charge. It seems to me altogether unnecessary, undesirable and moreover

[5] He might justly have omitted the word "animal."

impossible to draw a sharp line of distinction between the two sciences. With a common origin, mutual independence was, in time, necessary to the growth of each, yet this is in entire harmony with the fact that they have a common meeting-ground. In these days, as always, the morphologist must be something of a physiologist: the physiologist something of a morphologist. The current researches and discussions on evolution, heredity, and other fundamental questions make this constantly more evident. Like zoology and botany, each has its special field of labor, its special methods, and its special problems: but the fields are constantly overlapping, the one learns methods from the other, and the ultimate problems of both are the same.

Let us now draw together the main lines of our thesis. I prefer to conceive of physiology as the science of the dynamics of living matter. Its tasks for the future seem to comprise the following classes of investigations.

First, the functions of adult organs, tissues and cells in plants, Invertebrates and Vertebrates. The greatest interest at present appears to center about the phenomena of heredity, the central nervous system, and general cell physiology. Second, the ontogeny of functions, or embryological physiology. Third, the phylogeny of functions. Fourth, the physiology of organisms, comprising the mutual relations of organisms to each other and to their environment.

It would be superfluous here to discriminate between the opportunities for research offered in these four classes of problems. Each covers a wide field of rich promise. Each is largely unworked—in reality, as we have shown, research in the past has been confined almost wholly to the first group. Each will lead the investigator to fundamental problems.

In considering these tasks it will be perceived that I have viewed the organism in two aspects, in its internal and its external relations. The problems of the first three groups may be regarded as belonging to *internal physiology*, those of the fourth to *external physiology*. Nearly twenty-five years ago, Haeckel made a similar division into *Conservations-* and *Relations-Physiologie*.[6] Such a classification is convenient and valuable. But it must be remembered that it is artificial, and must not be taken as indicating a fundamental distinction between two sciences. The two are departments of the one

[6] *Jenaische Zeitschrift*, V, 1870.

science, physiology, and pass the one into the other. For a fact that becomes the more striking, the longer one studies the dynamics of living matter, is the utter impossibility of drawing a sharp line between the internal and the external. The functional organism is constantly acted upon by the environment, and is incapable of existence apart from it. But the functional organism is but the *ensemble* of the functional parts, and the parts are linked functionally together, constantly acting and reacting upon each other and modifying each other's work. It follows that the innermost portions cannot free themselves from environmental influence, and the attempt at an essential separation of internal from external physiology is in vain. Nor is such an attempt justified any the more by methods of investigation. For he who studies the action of light upon the retina, is thereby fitted to investigate the heliotropic phenomena of the organism; and he who is familiar with methods by which the effect of salts or temperature on the organs is tested, is most capable of testing the influence of the composition and the temperature of the surrounding water upon aquatic animals and plants. I speak of this the more especially because of the fact that, since the completion of the greater portion of this paper, the able address of Professor Burdon Sanderson, as President of the British Association for the Advancement of Science, has appeared.[7] In an interesting manner Professor Sanderson reviews the aspects of physiology since the time of Müller. He says, "The distinction . . . between the internal and external relations of plants and animals has, of course, always existed, but has only lately come into such prominence that it divides biologists more or less completely into two camps—on the one hand, those who make it their aim to investigate the actions of the organism and its parts by the accepted methods of physics and chemistry, carrying this investigation as far as the conditions under which each process manifests itself will permit: on the other, those who interest themselves rather in considering the place which each organism occupies, and the part which it plays in the economy of nature. It is apparent that the two lines of inquiry, although they equally relate to what the organism *does*, rather than to what it *is*, and therefore both have equal right to be included in the one great science of life, or biology, yet lead in directions which are scarcely even

[7] *Nature*, September 14, 1893.

parallel." Giving then a somewhat misleading interpretation of Haeckel's ideas above referred to, Professor Sanderson proceeds to divide Biology into three parts, Morphology, Physiology, which deals with the "internal relations of the organism," and Oecology (a term borrowed from Haeckel) "which concerns itself with the external relations of plants and animals to each other, and to the past and present conditions of their existence." In another place, Professor Sanderson says, "No seriously-minded person, however, doubts that organized nature, as it now presents itself to us, has become what it is by a process of gradual perfecting or advancement, brought about by the elimination of those organisms, which failed to obey the fundamental principle of adaptation, which Treviranus indicated. Each step, therefore, in this evolution, is a reaction to external influences, the motive of which is essentially the same as that by which, from moment to moment, the organism governs itself."

I realize how presumptuous it appears in me to differ from or attempt to criticise the views of one who occupies so deserved a place among the foremost physiologists of to-day. Yet I cannot repress the thought that the author of the Nottingham address viewed his subject more in the waning light of a day that is ending than in the brightening beams of a coming dawn. If each "step . . . in this evolution is a reaction to external influences," why should not the student of the "steps" study also the origin and causation of those steps? I think he would justly be open to the charge of narrowness if he did not do it. And, moreover, as I have indicated above, I believe not only that he of all is best fitted, but that a rational view of his science forces him to do it. The progress of a scientific physiology has been greatly retarded by its followers confining themselves too exclusively to "the internal relations of the organism." Not the least of the retarding consequences is the fact that thereby the science loses much of its attractiveness. Just as anatomy, illumined and vivified by the theory of evolution, and broadened by the incorporation of embryology and paleontology, became the science of morphology, so I believe that physiology is destined to undergo, and is undergoing, a similar vivifying and broadening process, and is to become the science of vital phenomena, wherever and however they may be exhibited.

Studies from the Department of Physiology of Columbia College at the College of Physicians and Surgeons New York. Vol. I. — Reprinted from the „Centralblatt für Physiologie" of the 11th August 1894.

Die zuckerbildende Function des N. vagus.

Von Dr. **P. A. Levene.**

Die directe Einwirkung des Nervensystems auf die Zuckerbildung in der Leber war bis vor sehr kurzer Zeit nur wenig erforscht. Alle früheren Untersuchungen haben eher auf ihren reflectorischen Charakter hingedeutet. Aber jüngst sind einige Arbeiten erschienen, welche einstimmig auf die zuckerbildende Function der Lebernerven hinweisen (Butte,*) Morat, Dufourt,**) Gebrüder Cavazzani).***) Alle diese Arbeiten, ausser der ersten, erschienen erst, nachdem ich meine Untersuchungen angefangen hatte.

Den Anlass, die zuckerbildende Function des N. vagus vorauszusetzen, gaben mir vor allen Dingen die von Claude Bernard angeführten Thatsachen, dass nicht nur die Reizung des centralen Endes des N. vagus Diabetes erzeugt, sondern auch die alternative Reizung des oberen und unteren Endes dasselbe Resultat ergeben und dass die Durchschneidung der Nn. vagi das Schwinden des Zuckers aus dem Organismus zur Folge hat, und endlich hat die Arbeit von Butte mich endgiltig veranlasst, mich mit der Untersuchung des directen Einflusses des N. vagus auf die Zuckerbildung in der Leber zu beschäftigen.

Meine zweite Aufgabe in dieser Arbeit war, der Quelle dieses Zuckers auf den Grund zu kommen; zu diesem Zwecke stellte ich einen Theil meiner Experimente an normalen Thieren und den anderen an hungernden an.

Ausser dem Zucker bestimmte ich das Glykogen nach Brücke-Külz und die Gesammtkohlenhydrate nach der Methode von Seegen in zugeschmolzenen Röhren. Ich muss hier bemerken, dass da, wo die Quantität des Glykogens unbedeutend war, die zweite Methode einen bedeutend höheren Werth ergab. Ich glaube annehmen zu dürfen, dass die Quelle der Verluste bei der Methode von Brücke-Külz bedeutend grösser ist. Die Reizung wurde vermittelst eines automatischen Schlüssels so regulirt, dass sie je eine Viertelminute wirkte und drei Viertelminuten unterbrochen war. Die nachfolgenden Tabellen stellen die Resultate meiner Experimente dar:

*) La Semaine Médicale No 11, 1894
**) Arch. de physiol. avril 1894.
***) Centralbl. Nr. 2, VIII, 1894.

Vers.-Nr.	Ohne Reizung: Thiergattung	Zucker in Procent	Glykogen in Procent	Gesammt-Kohlehydrate in Procent	Vers.-Nr.	Mit Reizung: Thiergattung	Zucker in Procent	Glykogen in Procent	Gesammt-Kohlehydrate in Procent
	Normale Thiere.								
I	Katze	1·11	1·00	4·54	IV	Katze	1·23	0·24	1·81
II	Katze	1·14	3·11	4·25	V	Katze	1·42	0·50	2·69
III		0·88	9·07	11·20	VI	Katze	1·30	1·40	3·95
					VII	Kaninchen	1·83	2·52	4·40
					VIII	Kaninchen	3·52	7·13	12·20
	Hungernde Thiere.								
IX	Katze	0·58	0·25	1·12	XII	Katze	1·00	—	1·78
X	Kaninchen	1·60	0·27	3·69	XIII	Kaninchen	2·50	0·25	4·20
XI	Kaninchen	—	0·50	3·42	XIV	Kaninchen	1·87	0·51	2·81
					XV	Kaninchen	2·56	1·0	3·58
					XVI	Kaninchen	2·62	0·70	5·23

Aus diesen Experimenten ist ersichtlich, dass die Reizung des N. vagus eine relative Vermehrung des Zuckers in der Leber normaler wie hungernder Thiere hervorruft und dass die Quantität des Glykogens (der Gesammtkohlehydrate) bei den normalen Thieren abnimmt. Bei den hungernden Thieren fand diese Verminderung der Gesammtkohlehydrate nicht statt.

Wenn wir nun in Betracht ziehen, dass der Zucker bei gesteigerter Production in grösseren Quantitäten ausgeführt wird, so müssen wir zum Schlusse gelangen, dass in der hungernden Leber bei Reizung des N. vagus thatsächlich eine Zunahme der Gesammtquantität der Kohlehydrate eintritt.

Um mich zu überzeugen, dass die Zuckerzunahme thatsächlich nicht mit der Gesammtabnahme der Kohlehydrate verbunden ist, untersuchte ich in einigen Fällen die Leber der hungernden Thiere sofort nach dem Ausschneiden und wieder nach einem kurzen Zeitraum.

Hier die Resultate:

Vers.-Nr.	Thiergattung	Zucker in Procent	Gesammtkohlehydrate in Procent	Zeit nach Ausscheidung	Zucker in Procent	Gesammtkohlehydrate
				Stunden		
I	Kaninchen	—	3·42	3	3·53	5·35
II	Kaninchen	2·62	5·23	6	3·48	7·14
III	Hund	0·74	1·26	6	0·76	1·25

Die Resultate der Experimente mit Reizung des N. vagus würden am besten bestätigt durch die von Claude Bernard mitgetheilte Thatsache, dass die Durchschneidung der Nn. vagi die Abnahme von Zucker in der Leber und im Blute erzeugt.

Leider gelang es mir nicht, in den drei von mir angestellten Experimenten dieselben Resultate zu erreichen. Ich fand Zucker in dem Blute und der Leber der Thiere am dritten Tage nach der Durchschneidung der Nerven, wobei die Reizung des N. vagus stets eine Zuckersteigerung im Blute erzeugte.

Hier werde ich auch ein Experiment an einem Hunde erwähnen, der eine ziemlich lange Zeit gehungert hatte; das Glykogen in der Leber verschwand fast gänzlich, die Reizung des N. vagus aber ergab eine Zuckervermehrung im Blute (S. IV).

Vers.-Nr.	Zucker im normalen Blute in Procent	Zeit nach Durchschneidung Tage	Zucker im Blute nach Durchschneidung in Procent	Zucker im Blute nach Reizung in Procent	Zucker in der Leber in Procent	Gesammtkohlehydrat in der Leber in Procent
I	0·133	1	0·130	—	0·81	—
II	0·140	2 3	0·120 0·131	0·170 0·177	1·58	3·15
III	0·150	— 3	— 0·144	0·208 0·184		
IV	0·072	—	—	0·139	0·74	1·26

Die Resultate meiner Arbeit sind im Allgemeinen die folgenden:

Die Reizung des peripherischen Endes des N. vagus steigert die Zuckerproduction in der Leber (die Durchschneidung des N. vagus erzeugt kein Zuckerschwinden im Organismus).

Bekanntlich sind über die Zuckerbildung in der Leber drei Ansichten geäussert worden: Claude Bernard sah in der Zuckerbildung eine einfache chemische Umwandlung des Glykogens in Zucker. Pavy sprach der Leber jede zuckerbildende Function ab und Seegen betrachtete als die Quelle des Zuckers nicht das Glykogen, sondern einzig das Eiweiss. Die Resultate meiner Experimente, wo wir eine ziemlich bedeutende Zunahme des Zuckers in der lebenden Leber haben, harmoniren augenscheinlich nur wenig mit der Ansicht Pavy's.

Was die zwei anderen Theorien betrifft, muss man bekennen, dass die Ansichten Claude Bernard's und Seegen's richtig sind, aber nur zum Theil, da einerseits die Zunahme des Zuckers parallel mit der Abnahme des Glykogens in die Leber normaler Thiere geht, andererseits es aber auch nicht bestritten werden kann, dass in der Leber hungernder Thiere die Zuckerbildung nicht auf Kosten des Glykogens stattfindet.

(Uebrigens ist es Claude Bernard selbst gelungen. Diabetes bei einem hungernden Hunde durch die Reizung des centralen Endes des N. vagus zu erzeugen.)

Zum Schluss ergreife ich die Gelegenheit, den Herren Professor J. G. Curtis und Dr. F. Lee meinen Dank für ihre freundliche Unterstützung bei meiner Arbeit auszusprechen.

Im Selbstverlage. – K. u. k. Hof- und Staatsdruckerei in Wien.

Studies from The Department of Physiology of Columbia College at the College of Physicians and Surgeons. Vol. I.

[Reprinted from the Journal of Physiology.
Vol. XVII. Nos. 3 & 4, Oct. 1894.]

A STUDY OF THE SENSE OF EQUILIBRIUM IN FISHES, PART II.

By FREDERIC S. LEE, Ph.D., *Columbia College, New York.* (12 Figures in Text.)

Contents.

I. Introduction.
II. Compensating Movements.
III. Reactions following Compensating Movements.
IV. The Acoustic Nerve.
V. The Semicircular Canals.
  1. Comparison of natural and artificial stimulation.
  2. Principal and subordinate functions.
VI. Summary of Results.

I. Introduction.

The present paper gives the results of further researches into the question of the equilibrium function of the acoustic nerve and forms a continuation of a paper already published[1]. The work was carried on during the summer of 1893, at the Marine Biological Laboratory, Wood's Holl, Massachusetts, U.S.A. All experiments here reported were performed upon the species heretofore studied, viz.: *Galeus canis* (Mitchill), the common smooth dog-fish. The methods employed were essentially the original ones; differences in details will be discussed in the appropriate sections. In the present series of experi-

[1] Part I. This *Journal*, xv. 311, 1893.

Corrigenda to Part I.

p. 333, in description of Fig. 11, for "3 *a*" read "3 *b*"; for "3 *b*" read "3 *a*."
p. 334, line 12, for "323, 324" read "331."
p. 336, line 9 from bottom, for "323, 324" read "330 and 333."
p. 337, line 3, for "upper" read "lower."

ments my aim has been to fill in certain gaps that were left in the previous series, to make the proof of certain points more logically complete, and experimentally to verify certain inferences and prophecies resulting from the theory formerly stated. In a word it may be said that the new results are entirely in harmony with the earlier ones, and, moreover, justify as correct the first statement of the theory.

II. Compensating Movements.

In the former paper the compensating movements of the eyes and fins, following passive rotation of the animal's body around the three chief body axes and through several degrees of arc, were described (movements 1 *a*, 1 *b*, 2 *a*, 2 *b*, 3 *a*, and 3 *b*). For movements in other planes it was simply stated that when the animal's body was "rolled simultaneously about two axes, the compensating movements are always a combination of the movements accompanying rotation separately about the same axes." In detail, there are here given the actual facts resulting from simultaneous rotations about the longitudinal and transverse axes, *i.e.* in the planes of the vertical semicircular canals.

4. When rolled in the plane of the left anterior and right posterior canals,

(*a*) head downward:

Left eyeball rolls upward, anterior pole more than posterior (Fig. 1, upper figures).

Right eyeball rolls downward, posterior pole more than anterior.

Left pectoral fin does not move.

Right pectoral fin bends strongly upward.

Dorsal fin bends to the left.

The compensating positions of eyes and fins are maintained when the body is held in the new position.

The rotation of the body in the plane of the two canals (4 *a*) is really a combination of the two rotations about the longitudinal axis and the transverse axis respectively (1 *a* and 3 *a* of Part I); and, as might have been predicted, the movements of both eyes and fins are seen to be combinations of the movements obtained in rotations 1 *a* and 3 *a*; *e.g.* in 1 *a* the left eyeball rolls straight upward, in 3 *a* its anterior pole upward; while in 4 *a* the upward movement and the rotation about the visual axis are combined. The combination of fin movements is especially striking:

e.g. in 1 *a*,

The left pectoral fin bends downward.
The right pectoral fin bends upward.
The dorsal fin bends to the left.

In 3 *a*,

The left pectoral fin bends upward.
The right pectoral fin bends upward.
The dorsal fin does not move.

In 4 *a*, the movement of each fin is the algebraic sum of these. This is most markedly shown by the left pectoral; when the rotation of the fish is exactly in the plane of the canal in question, there is no movement of this fin; when the plane of rotation is varied toward 1 *a*, there is a downward movement; when toward 3 *a*, an upward movement; in each case the amount of movement increases with the divergence of the plane of rotation from the plane of the canal. No special attention was given to the posterior dorsal, anal, and pelvic fins, since the compensating movements of all of these are very slight.

If Fig. 1 (upper figures) be compared with Fig. 6 of Part I. it will be seen that the eye movements resulting from passive rotation in the plane of the left anterior canal toward its ampulla and those resulting from artificial stimulation of the left anterior ampulla are the same. The statement on page 329 of Part I, that "these movements [upon stimulation]...are exactly what would be expected to result from movement of the normal body in the plane of the canal whose ampulla is stimulated," is hence proved experimentally to be correct. And, moreover, the inference is completely and unequivocally justified that, when a fish in swimming dives downward and to the left, the left anterior canal is *par excellence* the sense-organ that appreciates the movement.

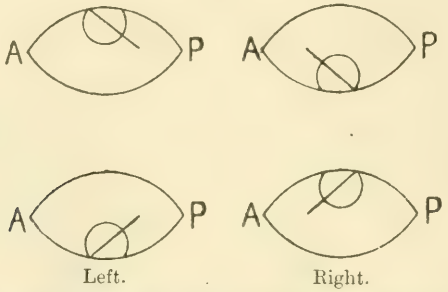
(*b*) head upward:

Left eyeball rolls downward, anterior pole more than posterior (Fig. 1, lower figures).
Right eyeball rolls upward, posterior pole more than anterior.
Left pectoral fin does not move.
Right pectoral fin bends strongly downward.
Dorsal fin bends to the right.
Maintenance of the compensating positions is as in 4 *a*.

Exactly similar considerations apply here as under 4 *a*, the combination in 4 *b* being that of 1 *b* and 3 *b*. The results harmonize with those obtained by artificial stimulation of the right posterior canal, and

experimental justification is given to the inference from the previous experiments that "the function of this canal...is the appreciation of movements in its own plane toward its ampulla" (page 332, Part I).

Fig. 1.



Compensating positions of eyes for body positions 4 *a* (upper figures) and 4 *b* (lower figures). The figures in the present article are constructed on the same plan as those in Part I; *i.e.* the left eye is represented as seen from the outside, the right as seen from the median side; the straight lines indicate the true horizontal plane of the eyeballs.

5. When rolled in the plane of the right anterior and left posterior canals,

(*a*) head downward:

Left eyeball rolls downward, posterior pole more than anterior (Fig. 2, upper figures).

Right eyeball rolls upward, anterior pole more than posterior.

Left pectoral fin bends strongly upward.

Right pectoral fin does not move.

Dorsal fin bends to the right.

Upon holding the body in the new position, the compensating positions are maintained.

These results are a combination of those of 1 *b* and 3 *a* and demonstrate the prepotency of the right anterior canal in the given rotatory movement. Cp. Fig. 7 of Part I.

(*b*) head upward:

Left eyeball rolls upward, posterior pole more than anterior (Fig. 2, lower figures).

Right eyeball rolls downward, anterior pole more than posterior.

Left pectoral fin bends strongly downward.

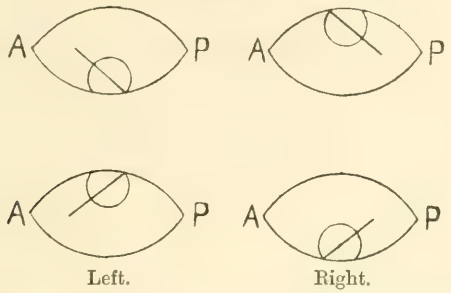
Right pectoral fin does not move.

Dorsal fin bends to the left.

Maintenance is as in 5 *a*.

Here is a combination of movements 1 *a* and 3 *b*. The left posterior canal is the functional sense-organ. Cp. Fig. 10 of Part I.

Fig. 2.



Compensating positions of eyes for body positions 5 *a* (upper figures) and 5 *b* (lower figures).

Upon any other theory than the one advocated in the present research it would be difficult, I think, to explain understandingly the curious compensating movements that are found to accompany rotations 4 and 5. Looked at, however, in the light of the hitherto observed and reported facts, they are clear. Each rotation may be regarded as a compound movement, made up of simple rotations around two of the chief body axes. When such a complex rotation is analysed into its elements, and the compensations of the latter are observed in the living animal, then it becomes a simple mathematical problem to compute the more complicated compensations of the former. As a matter of fact the compensations of rotations 4 and 5 were actually predicted; and subsequent testing of the matter in the normal animal proved the complete identity of the predictions and the observed facts. This mathematical harmony between the various facts of observation gives the very strongest support to the proposed theoretical explanation of them. Evidently each vertical canal acts as a sense-organ of dynamical equilibrium for rotatory movements of the animal's body in its own plane and toward its own ampulla. The maintenance of the compensating positions of eyes and fins while the animal is at rest in positions 4 and 5, as in 1 and 3, indicates that here statical organs are at the same time in function. As regards the actual length of time during which maintenance of the compensating positions continues, little can be said. No fish will compensate actively and well after a few minutes, when taken out of the water and held in the hand or on the shark-board without artificial respiration, as in all my experiments

on normal compensation. When he is held at rest in abnormal attitudes, maintenance of compensation continues sometimes for several seconds only, the eyes and fins both returning gradually to their customary resting positions of least tension.

III. Reactions following Compensating Movements.

I come now to a portion of the subject that, for the sake of clearness, I have thought best heretofore entirely to omit. In discussing the compensating movements it has been stated that, if the body of the normal fish be turned into any one of the ten positions studied and be held there at rest, in positions $2a$ and $2b$ (*i.e.*, movements in the horizontal plane) the eyes and fins return to their normal resting positions, while in all other positions, $1a$, $1b$, $3a$, $3b$, $4a$, $4b$, $5a$, and $5b$ the compensating positions of the eyes and fins are maintained. This has been regarded and without doubt rightly so, as indicative of the presence and action of statical organs of equilibrium, probably represented by the otolithic parts of the ears. The bare mention of a maintenance of the compensation, or of the return to the normal resting position, however, does not tell the whole story. All the facts resulting from my experiments lead to the belief that the normal stimulation of any *crista acustica* is effected by the inertia of the endolymph. As the canal is rotated, the projecting sensory hairs are dragged through the inert endolymph and a nerve impulse results. If this be so, we should expect *a priori* upon stoppage of the rotation a reactionary movement of the hairs, resulting in a reactionary stimulus and hence a corresponding reactionary movement of the eyes and fins succeeding the normal compensation. While the compensation represents the activity of the principal function of the canal or pair of canals, the reaction would represent that of the subordinate function[1].

Now as a matter of fact such reactions of eyes and fins, perfectly distinct and uniform, do actually occur. They follow immediately upon the compensation and consist always of a movement in a direction opposite to it. They are thus in every case an approach to the normal resting position. They are always slight, always less than the com-

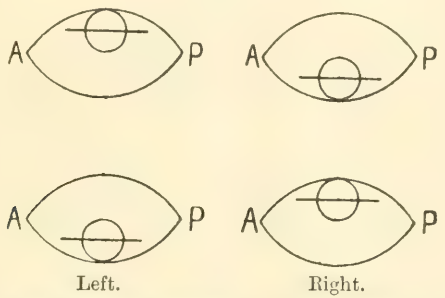
[1] It is to be noticed that I omit here entirely the consideration of the so-called functional opposite, and limit the discussion to the canal or canals toward which the rotatory movement is directed. It will be remembered that in Part I, I gave experimental evidence tending to show that, when one canal or pair of canals is acting, its functional opposite is also acting. This means that during the principal activity of the former, the subordinate activity of the latter is in operation and *vice versa*. I prefer to obtain more experimental data before taking up this question exhaustively.

pensation, except, as stated, in 2 *a* and 2 *b*, where complete return to the normal position of rest ensues. In all cases, however, the actual maintained position is the position of compensation minus the reaction.

Like the compensations the reactions and maintenance of the positions of the fins are inclined to be less constant and satisfactory than are those of the eyes. Upon being taken from the water a fish naturally resists with voluntary movements of the trunk and limbs. These last usually for a few seconds only. On the other hand, too long exposure of the body to the air and repeated tilting in various directions render the fin movements sluggish. Careful delicate manipulation and the employment of fresh animals show, however, that the above laws hold good for the fins as for the eyes.

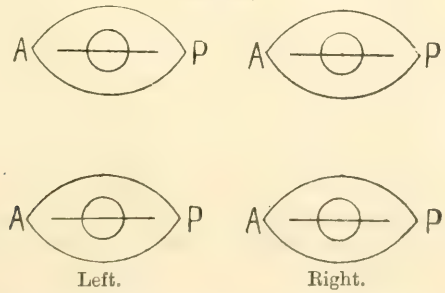
The reactions of the eyes for the ten body positions are seen at once by a comparison of the figures of normal eye compensations (Figs. 3, 4, and 5 of Part I and Figs. 1 and 2 of the present article) with the following figures of maintained eye positions.

Fig. 3.



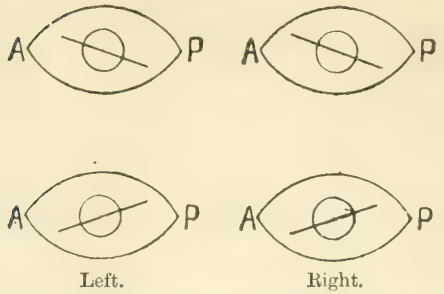
Resting positions of eyes for body positions 1 *a* (upper figures) and 1 *b* (lower figures). *i.e.* diminution of compensation but no return to normal. Compare with Fig. 3 of Part I.

Fig. 4.



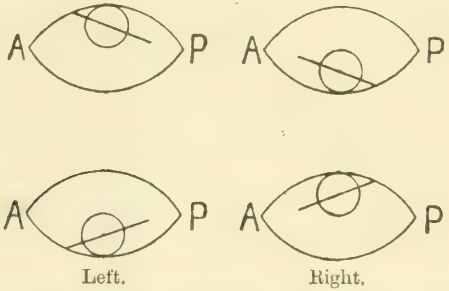
Resting positions of eyes for body positions 2 *a* (upper figures) and 2 *b* (lower figures). *i.e.* diminution of compensation amounting to complete return to normal. Compare with Fig. 4 of Part I.

FIG. 5.



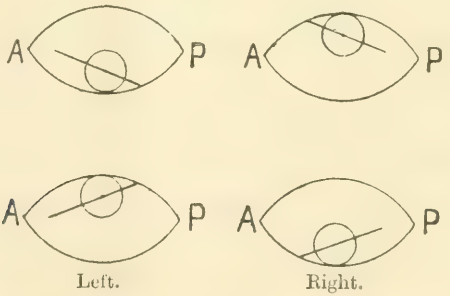
Resting positions of eyes for body positions 3 *a* (upper figures) and 3 *b* (lower figures). *i.e.* diminution of compensation but no return to normal. Compare with Fig. 5 of Part I.

FIG. 6.



Resting positions of eyes for body positions 4 *a* (upper figures) and 4 *b* (lower figures). *i.e.* diminution of compensation in both vertical and rotatory movements but no return to normal. Compare with Fig. 1 of present article.

FIG. 7.



Resting positions of eyes for body positions 5 *a* (upper figures) and 5 *b* (lower figures). *i.e.* diminution of compensation in both vertical and rotatory movements but no return to normal. Compare with Fig. 2 of the present article.

These reactions scarcely need discussion. That they are always in

a direction opposite to the compensation is the important fact concerning them, and this is to be correlated with the physical fact that sudden stopping of the rotating body must give to the *crista acustica* concerned an impulse in a direction opposite to that given by the rotation. Taken by themselves the reactions may perhaps not be regarded as proving the existence of a subordinate function belonging to each ampulla. Taken in connection with the results of stimulation about to be reported, however (see below, V. 2), it may not be doubted that they are the visible expression of subordinate functions.

The leading equilibrium events then that accompany a partial rotation of a fish's body in any plane, together with their physiological relations are as follows:—

1. Compensation of eyes and fins: principal activity of semicircular canal or canals.
2. Reaction of eyes and fins: subordinate activity of semicircular canal or canals.
3. Maintenance of eyes and fins: activity of statical organ or organs.

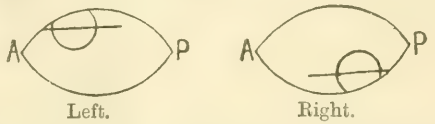
As above stated, the question of the simultaneous activity of the functionally opposite canal or pair of canals is here left out of consideration.

IV. The Acoustic Nerve.

In Part I the results of cutting one or both acoustic nerves were reported and discussed. I have now to add the effects of artificial stimulation of this nerve. So far as I am aware, the experiment, though an easy one, has not before been done. The method of procedure is to open the auditory capsule from above, remove the contents, cut the nerve across where it begins to split up into its branches, and then apply electrodes to the stump. I have used electrical stimulation only, an induction current from a du Bois coil. The results accord entirely with the stimulation experiments on the various branches of the nerve. They vary with the position of the electrodes upon the stump. If these are placed more on the anterior side in the vicinity of the external fibres and not too strong a current is used, the effect is the same as that which results from stimulation of the external ampullar branches of the acoustic, viz.:—for left stimulation, the left eyeball rolls anteriorly, the right eyeball posteriorly (compensating position $2a$ or Fig. 15 of Part I). If the electrodes are placed more upon the posterior side of the nerve trunk, pure posterior effects follow, viz.:—for left

stimulation, the left eyeball rolls upward, posterior pole more, the right eyeball rolls downward, anterior pole more (compensating position 5 *b* or Fig. 10 of Part I). I have never succeeded in demonstrating by this method unadulterated anterior effects, doubtless because I have never succeeded in confining the stimulating current to anterior fibres alone. But touching the exposed stump has at times given a combination of anterior and posterior effects, viz.:—for left stimulation, the left eyeball rolls straight upward, the right eyeball straight downward (compensating position 1 *a*, Fig. 3 of Part I). Lastly, if the two platinum electrodes be separated sufficiently to allow the trunk of the nerve to lie between them and a moderately strong stimulating current to reach all the fibres, we have the most beautiful result of a combination of anterior, posterior, and external effects, viz.:—for left stimulation, a rolling of the left eyeball strongly upward and at the same time somewhat forward, of the right eyeball strongly downward and somewhat backward (Fig. 8), a bending of the left pectoral fin downward, of the right pectoral fin upward and of the dorsal fin to the left. *All these changes in position are the exact reverse of those following section of the same nerve.*

Fig. 8.



Position of the eyes upon stimulation of the left acoustic nerve.

These results of total acoustic stimulation do not surprise us when they are compared with those of stimulation of the various branches of the acoustic nerve, ampullar and otolithic, reported in Part I. No new movements are brought out by the later experiments. Those that actually occur are the resultants of the combined reflexes proper to the component parts of the whole nerve. The complete antagonism of the effects of stimulation and of section is most striking. It settles conclusively the dispute as to whether cutting the nerve stimulates or paralyzes its component fibres. The question of sensations of equilibrium in the cases of section and of stimulation is an interesting but highly complicated one. I shall postpone the discussion of it, however, until more shall have been learned experimentally of the mode of working of the otolithic organs.

It will be observed that all the results of stimulating the acoustic nerve here reported are those which indicate the activity of the principal

function of the nerve. For our present purpose these are of the most importance. I have not yet endeavoured by artificial stimulation to bring out the subordinate function of the nerve as a whole.

V. The Semicircular Canals.

From a large number of facts observed in connection with the stimulation and section of the various ampullar branches of the acoustic nerve and reported in Part I, a theory of the physiology of the canals was proposed. A few points were not wholly proved, so far as proof consists in the marshalling of actually observed facts rather than of inferences however strong.

The results of further experimental work along the same lines I present here under two headings.

1. *Comparison of natural and artificial stimulation.*

One assumption that I made in my former article was that artificial stimulation of the nerve branches gives results entirely similar to those of natural stimulation. This was actually established experimentally for the external canals. Inasmuch, however, as some critics may object to the drawing of such an inference from so few data, I have carried out a series of experiments to prove positively the validity of the reasoning. A part of the proof has already been given on pages 194—196. It was there pointed out that mechanical stimulation of the left anterior ampulla, right anterior ampulla, left posterior ampulla and right posterior ampulla, produces reflex movements of the eyes and fins identical with those following the tipping of the body of the normal living fish in the planes of the respective canals toward their ampullæ. These facts speak for themselves.

Equally conclusive are the facts obtained by simultaneous stimulation of two ampullæ. It will be remembered that we have evidence of the functional pairing of the various canals with each other. Any two canals not lying in the same plane may together act as a sense-organ for the appreciation of rotational movements of the body in planes lying between them. When the plane of rotation is midway between the planes of the two canals, the latter act to an equal extent; when the plane of rotation lies more nearly parallel to the plane of one canal than the other, the one canal predominates over the other. Thus the two anterior canals together appreciate forward rotatory movements in the sagittal plane, or in other planes lying between them; the two posterior

canals appreciate backward rotatory movements in the same planes; the anterior and posterior canals of the same side together appreciate movements in frontal and other planes lying between them. In the case of each pair the mathematical combination of the results of stimulating artificially and separately the two component ampullæ gives results exactly like those of natural stimulation of the double sense-organ. But simultaneous artificial stimulation of the two ampullæ was never tried. This has now been done so far as the two anterior, the two posterior, the anterior and posterior of the same side and of opposite sides, and the two external canals are concerned. In each of these cases the stimulation was mechanical and consisted of moderate pressure upon the surface of the exposed ampulla by a blunt needle held in the hand. This method is very effective, even although it affords no means of measuring accurately the intensity of the pressure and hence affords no possibility of equalizing at will the two simultaneous stimuli. Indeed it would be difficult to find a method short of the natural one that would allow of this. It follows hence that upon such simultaneous stimulation of two ampullæ in successive trials the experimenter obtains either the desired combined action of the two *cristæ acusticæ*, or the more pronounced action of the one or the other, according as both are stimulated equally or unequally. Leaving the cases of unequal stimulation out of account as immaterial to our present purpose, we can sum up our results as follows:

Simultaneous artificial stimulation of the two anterior ampullæ causes both eyeballs to roll their anterior poles upward, their posterior poles downward. This movement is the same as that which results from natural stimulation or from rotating the animal about the transverse axis head downward (3 *a*, Fig. 5, upper figures, Part 1). It is, moreover, the algebraic sum of the movements following separate artificial or natural stimulation of the two anterior ampullæ.

Simultaneous artificial stimulation of the two posterior ampullæ causes both eyeballs to roll their anterior poles downward, their posterior poles upward. This movement is the same as that resulting from natural stimulation or from rotating the animal about the transverse axis head upward (3 *b*, Fig. 5, lower figures, Part 1). It is also the algebraic sum of the movements following separate artificial or natural stimulation of the two posterior ampullæ.

Simultaneous artificial stimulation of the anterior and posterior ampullæ of the same side causes the eyeball of that side to roll straight upward, that of the opposite side straight downward. This movement

is the same as that resulting from natural stimulation or from rotating the animal about the longitudinal axis toward the same side (1 *a* or 1 *b*, Fig. 3, Part 1). It is also the algebraic sum of the movements following separate artificial or natural stimulation of the same ampullæ.

Simultaneous artificial stimulation of the anterior and posterior ampullæ of opposite sides causes no movement of the eyeballs, *i.e.* the action of one ampulla completely neutralizes the action of the other or, in other words, the algebraic sum of the movements following separate artificial or natural stimulation of the two ampullæ in question equals zero. Simultaneous natural stimulation of the two ampullæ is impossible; the fish cannot turn in two opposite directions at the same time.

Simultaneous artificial stimulation of the two external ampullæ causes no movement of the eyeballs, *i.e.* the action of one ampulla completely neutralizes the action of the other, or, in other words, the algebraic sum of the movements following separate artificial or natural stimulation of the two ampullæ in question equals zero. Simultaneous natural stimulation of the two ampullæ is impossible.

It will be observed that in each of these cases attention was directed to the principal function of the pair of canals. Study of the subordinate function will be reported upon in Sect. 2 below. Observations of the fin movements have not yet been recorded. The results are clean-cut and are, it seems to me, a complete answer to the question of natural versus artificial stimulation. The reflex actions in the two cases are identical. Hence all that was stated or presumed in Part 1 regarding the probable results of simultaneous stimulation of two ampullæ is confirmed. Fig. 14, for example, represents now rather the actual "position of eyes" etc. than "the presumed position of eyes" etc.

2. *Principal and subordinate functions.*

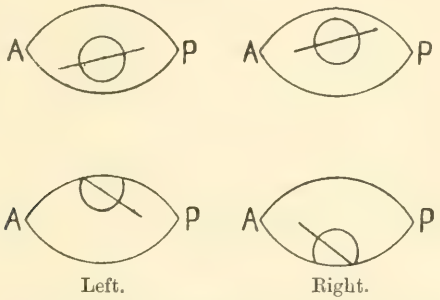
It will be remembered that the results of cutting the acoustic nerve of one side led to the belief that each nerve possesses a principal and a subordinate function in relation to equilibrium, the former dealing with motions toward the side of the body on which the nerve lies, the latter with motions toward the opposite side. This belief was strengthened by the analogous results of cutting the various ampullar branches of the nerve. Evidence was obtained to show that each separate canal, as well as each functional pair of canals, has a principal and a subordinate function. As regards the quality of the reflex actions that may result from the principal and from the subordinate activity respectively of any one canal or pair, they are in all respects the counterparts of each other.

Moreover, the principal function of one canal or pair is the same as the subordinate function of the functionally opposite canal or pair. Further evidence for the theory of subordinate functions has been reported in the present paper (pages 197 to 200). If, however, each canal does possess a double function, it ought to be possible to obtain still more complete and convincing proof, namely, by artificial stimulation. A considerable portion of the last summer's work has been devoted to this question. The task was so to stimulate artificially the hair cells, that at will the normal compensating action or the normal reaction should be brought out. As we have seen, the former was not difficult. Both electrical and mechanical stimulation—the only methods employed—readily called out the customary compensating movements of eyes and fins. With the reaction the matter was not so simple. The doctrine of specific nerve energies impels us to believe that two functionally different groups of nerve endings are present in each *crista*; one of which is predominant over the other. By artificial means to reach the subordinate without putting into activity the dominant group was not without difficulties. Several methods were employed. An approach to the natural conditions was attempted by inserting a pipette into the membranous canal and alternately forcing and drawing sea-water through the ampulla. Theoretically this would seem the ideal mode of testing the matter; and practically it did give the desired result. But, because of certain technical difficulties, it was not completely perfected in the time and with the laboratory facilities at hand and it was finally abandoned. Electrical stimulation was tried and found unsatisfactory. Lastly, the previously used method of mechanical stimulation by touching the surface of the exposed ampulla with a blunt needle was resorted to. This has given unequivocal results. It has been found possible to obtain from one and the same ampulla repeatedly and at will either action or reaction, either principal or subordinate activity. In a given case the function called forth seems not to be determined by the part of the ampulla that is touched but rather by the intensity of the stimulation employed; moderate and strong pressure invariably calls forth the principal function, very slight pressure the subordinate one. As the theory demands, the eye movements with the former are considerable, with the latter slight.

Thus barely touching the exposed surface of the anterior ampulla causes the eyeball of that side to roll slightly but distinctly downward, the anterior pole more than the posterior, while the eyeball of the opposite side rolls slightly upward, the posterior pole more than the

anterior (Fig. 9, upper figures. A comparison of this figure with Fig. 1, lower figures, shows that the results of the subordinate activity of the anterior canal are the same in kind as those of the principal activity of the functionally opposite canal). A stronger pressure brings out the exactly opposite and usual reaction, viz.:—the eyeball of the stimulated side rolls strongly upward, the anterior pole more, the opposite eyeball strongly downward, the posterior pole more (Fig. 9, lower figures). The former represents the subordinate, the latter the principal activity.

Fig. 9.



Positions of eyes upon very slight stimulation (subordinate function, upper figures), and stronger stimulation (principal function, lower figures) of the left anterior ampulla.

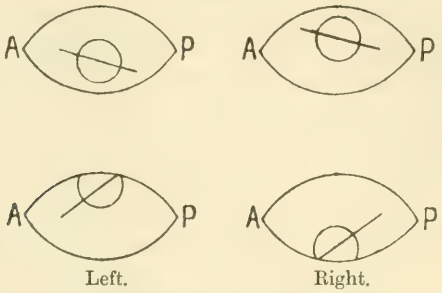
Barely touching the surface of the posterior ampulla causes the eyeball of that side to roll slightly but distinctly downward, the posterior pole more, the opposite eyeball slightly upward, the anterior pole more, which movements represent the subordinate activity (Fig. 10, upper figures. Cp. functional opposite, Fig. 2, upper figures). Stronger pressure causes the usual exactly opposite result, viz.:—the eyeball of the stimulated side to roll strongly upward, the posterior pole more, the opposite eyeball strongly downward, the anterior pole more, *i.e.*, the principal activity (Fig. 10, lower figures).

The external canals have given analogous, though not yet so entirely certain results. The external ampulla seems in all cases thus far tried excessively sensitive and the subordinate function has been brought out rarely.

As regards pairs of canals good reactions have been obtained from the anterior and the antero-posterior pair, the only ones tried. With the former the usual result of simultaneous moderate or strong stimulation applied to the two ampullæ equally (principal function) is given on page 203 of the present article, and in Fig. 5, upper figures, of Part I.

By using extremely slight pressure, however, it is possible to obtain quite the opposite effect, viz.:—in both eyeballs the anterior poles

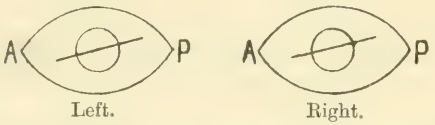
Fig. 10.



Positions of eyes upon very slight stimulation (subordinate function, upper figures) and stronger stimulation (principal function, lower figures) of the left posterior ampulla.

slightly downward, the posterior poles slightly upward, which movements represent the subordinate activity (Fig. 11. Cp. functional opposite, Fig. 5, lower figures, Part 1).

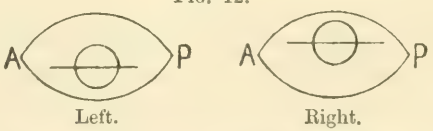
Fig. 11.



Position of eyes upon very slight simultaneous stimulation of the two anterior ampullæ (subordinate activity).

With the antero-posterior pair of canals the principal function is considered upon pages 203—204 of the present article and in Fig. 3, Part I. It is possible, however, so to modify the pressure in stimulation that exactly the opposite movement follows, viz.:—for left stimulation, the left eyeball moves slightly downward, the right eyeball slightly upward (Fig. 12. Cp. functional opposite, Fig. 3, lower figures, Part I).

Fig. 12.



Position of eyes upon very slight simultaneous stimulation of the left anterior and posterior ampullæ (subordinate activity).

With the anterior and posterior canals of opposite sides it has been shown that simultaneous equal stimulation, such as to call forth the

principal function of each ampulla, causes no movements of the eyes. It is obvious that similar antagonism and hence no movement accompanies the simultaneous subordinate activity of the two functionally opposite canals.

Experimental evidence of the possession by each ampulla of both a principal and a subordinate function hence seems abundant. In each of the cases above cited, either of single or paired canals, moderate or strong stimulation brought out movements of the eyes in a certain direction and of a certain intensity; slight stimulation yielded movements *in the exactly opposite direction and of a less intensity.* The results are definite and clean-cut, the facts are indisputable, and the terms, principal and subordinate functions, seem wholly justified.

VI. Summary of Results.

I have observed the compensating movements made by the eyes and fins of *Galeus canis* when the animal's body is turned (*e.g.* through 45° of arc) about any one of five different axes and in the planes of the various semicircular canals or in intermediate planes.

As regards the semicircular canals the planes and directions of rotation are :—

1st. The plane of the left anterior and right posterior canals; toward the former (4 *a*) and toward the latter (4 *b*).

2nd. The plane of the right anterior and left posterior canals; toward the former (5 *a*) and toward the latter (5 *b*).

3rd. The plane of the external canals; toward the left (2 *a*) and toward the right (2 *b*).

4th. The vertical plane that is midway between the planes of the two anterior canals, and of the two posterior canals; toward the former (3 *a*) and toward the latter (3 *b*).

5th. The vertical plane that is midway between the left anterior and posterior canals, and the right anterior and posterior canals; toward the left (1 *a*) and toward the right (1 *b*).

For each of these ten different rotations definite and characteristic compensating movements result. Rotations 4 *a*, 4 *b*, 5 *a*, 5 *b*, 2 *a*, and 2 *b* are in the planes of canals. Rotations 3 *a*, 3 *b*, 1 *a*, and 1 *b* are in planes intermediate between canal planes, and it is a significant fact that in each of these latter cases the compensating movements are the algebraic sum of the movements peculiar to the planes of the canals upon each side of the intermediate plane, just as in the parallelogram of forces any

one force may be regarded as a diagonal between two forces acting in two directions at an angle to each other. If the rotation be suddenly stopped and the animal's body be held at rest in the new position, a reaction is caused in the eyes and fins. Such a reaction consists in a diminution of the compensation, a movement toward the customary resting position. In no rotations in vertical planes is the resting position reached, at least with the eyes; the movements of the fins are apparently less constant and marked, and have not yet been studied so fully; in the horizontal plane there is a complete return of both eyes and fins to the normal position of rest.

All these movements may justly be regarded as connected with the maintenance of the equilibrium of the body. As such they are recognised in all the higher animals including man; and as such they may be considered as an index of the state of equilibrium of the body at the given moment.

That the organs of sense whose activity gives rise to the movements exist in the ampullæ of the semicircular canals has been proved by the results of operative experimentation. Such experimentation has been of two kinds, that of stimulating, chiefly mechanically, the exposed ampullæ and noting the results, and that of cutting the nerve supplying the ampullæ and then studying the equilibrium capacities of the animal. As regards the former method, I have stimulated with both strong and weak influences each ampulla by itself, and in pairs the two anterior, the anterior and posterior of the same side, and the anterior and posterior of opposite sides. In the case of a single ampulla I find the results of strong stimulation to be identical with the compensating movements accompanying rotation in the plane of the corresponding canal toward its ampulla; the results of weak stimulation are of an exactly opposite character and are those of the reactions following the same compensating movements. In the case of the two anterior ampullæ or the anterior and posterior of the same side I find strong stimulation to produce movements identical with the compensations accompanying rotation in the plane intermediate between the planes of the two canals in question and toward their ampullæ; weak stimulation on the other hand produces exactly opposite effects, identical with the reactions proper to the same rotations in the normal animal. In the case of the diagonally opposite anterior and posterior ampullæ properly graduated simultaneous stimuli, either strong or weak, produce no effects whatever, the movements resulting from stimulation of one ampulla evidently neutralizing those from stimulation of the other. In

each of the above cases, strong stimulation has called into play what I have called the principal function of the canal or ampulla, weak stimulation, the subordinate function. In the case of each canal or pair of canals, results of subordinate activity are qualitatively the same but quantitatively not so great as those of the principal activity of the functionally opposite canal or pair of canals. The results of artificial stimulation being identical with the compensations and reactions accompanying rotatory movements of the normal animal, it follows that we are justified in ascribing such compensations and reactions to the semicircular canals and in believing that the canals are the sense-organs of dynamical equilibrium. A rotational movement of the animal in the plane of any canal and toward its ampulla must stimulate the nerve endings and call forth the principal function of that canal and the subordinate function of the functionally opposite canal. Likewise a movement in a plane intermediate between the planes of two canals calls into action the combined principal functions of these two canals and the subordinate functions of the functionally opposite pair. The observations and experimental results reported in the present paper agree with and strengthen greatly the conclusions stated in Part I. The results of cutting the various ampullar branches of the acoustic nerve were reported in Part I, and harmonize beautifully with the above facts. It is clear that all such results of section may be explained by supposing the cutting operation to deprive the animal of all the sensory functions that I have ascribed to the canal or pair of canals the nerves of which have been cut.

In the present paper I have added to the proof of the function of the acoustic nerve by showing that electrical stimulation of the trunk of this nerve produces movements of the eyes and fins, that are the algebraic sum of the movements resulting from separate stimulation of the three ampullar branches and, moreover, are the exact reverse of the movements following section of the nerve.

The above comprise in brief the main results yet arrived at. For a concise statement of the function and mode of action of the canals, the reader is referred to pp. 344—347 of Part I.

Studies from The Department of Physiology of Columbia College at the College of Physicians and Surgeons, New York. Vol. I.

[Reprinted from the Journal of Physiology.
Vol. XVII. Nos. 3 & 4, Oct. 15, 1894.]

STUDIES IN PHLORIDZIN GLYCOSURIA.

By P. A. LEVENE, M.D.

(*From the Department of Physiology of Columbia College at the College of Physicians and Surgeons, New York.*)

The glycosuria that appears after the use of phloridzin raises many points that are of value in elucidating the subject of sugar formation. This drug produces a glycosuria which, as all agree, is due to increased production and not to diminished consumption of sugar within the organism, and has its source in the proteids of the body.

Further, phloridzin glycosuria upsets the idea of the exclusive or predominating activity of the liver in sugar formation, and has attracted the attention of physiologists to the part played by the kidneys in producing diabetes.

Phloridzin glycosuria has been produced after extirpation of the liver in geese (Thiel[1]), after ligature of the hepatic duct (Wolkow) and after fatty degeneration of the liver (v. Mering). Diabetes as a result of kidney disease was first asserted by C. Schmidt in 1850. Since then the co-existence of diabetes and albuminuria has been frequently brought forward. Armani and Farraro have described hyaline degeneration in the epithelium of Henle's sheath, and Ebstein has found necrosis in the epithelium of the convoluted tubules.

In a remarkable research Ehrlich described glycogenic degeneration of the epithelium of the tube of Henle, and Straus in the main confirmed the observation. Both regarded the degeneration as a secondary one.

v. Mering was the first to suggest the participation of the kidneys in the production of phloridzin glycosuria. Minkowsky advanced the explanation that phloridzin was decomposed in the kidneys, and that the phloretin thus liberated became again united to sugar in the organism,

[1] See bibliography at end of article.

the compound so formed being again broken up in the kidneys. Uschinsky also urges strongly that the kidneys participate actively in the production of diabetes, though in my opinion he goes too far when he suggests that they do so in all forms of that disease.

In order to solve more exactly the problem of the part played by the kidneys in the formation of glycosuria I undertook during the past year a series of experiments upon the action of phloridzin on dogs. In all cases the phloridzin was administered hypodermically and during all operations referred to in this paper ether was used as an anaesthetic. I began by giving the drug and repeating the operation of ligating the blood vessels of the kidneys. I estimated the sugar in the blood of the carotid artery before and after the operation, which was performed by means of the lumbar incision. The separation of the proteids of the blood was accomplished by a saturated solution of sodium sulphate. To 80 c.c. of a saturated solution of sodium sulphate was added directly from the blood-vessel about 20 grammes of blood. (The amount of blood was determined by weight.) A few drops of acetic acid were added, and the mixture was heated until all the proteids were coagulated. The mass was then filtered; the precipitate was washed with a hot saturated solution of sodium sulphate; and the washings and filtrate were tested for proteids and albumoses. They were usually absent. The sugar was then determined by the usual volumetric method with Fehling's solution.

My experiments have fallen naturally into four groups.

Group A.

This group comprises the experiments on the effect upon the sugar of the blood of ligation of the renal blood vessels after the administration of phloridzin.

Exp. I. Dog, 5·8 ks. in weight. Blood was taken from the carotid artery and the amount of sugar in it was found to be 0·120 %. 1·5 grs. of phloridzin were then injected. At 10 a.m. of the next day the amount of sugar in the blood of the carotid was 0·089 %. The blood vessels of both kidneys were then tied. At 4 p.m. the blood was again examined and the amount of sugar was found to be 0·078 %.

Exp. II. Dog, 5·6 ks. in weight. The carotid blood in its normal state contained 0·170 % of sugar. 0·75 gr. of phloridzin was injected. On the next day the amount of sugar in the blood was 0·109 %. The dog had eliminated in the meantime 160 c.c. of urine of sp. gr. 1050 and containing

3·3 % of sugar. The blood vessels and ureters of both kidneys were ligated in the morning at 10 o'clock. At 5 o'clock p.m. the blood was again examined and 0·121 % of sugar was found.

Exp. III. Dog, 6·7 ks. in weight. The carotid blood in its normal state contained 0·101 % of sugar. 1 gr. of phloridzin was injected. On the next morning the blood contained 0·106 % of sugar. In the meantime the dog had eliminated 800 c.c. of urine of sp. gr. 1050 and containing 6·25 % of sugar. The blood vessels of both kidneys were ligated at 10 o'clock a.m.; at 4 o'clock p.m. the amount of sugar in the blood was 0·209 %.

Exp. IV. Dog, 1·56 ks. in weight. At 9 a.m. the normal carotid blood contained 0·087 % of sugar. The blood vessels of both kidneys were then ligated and 2 grs. of phloridzin were injected at once. At 5 p.m. the blood contained 0·075 % of sugar; at 9 a.m. on the next day 0·064 %.

Exp. V. Dog, 5·7 ks. in weight. The blood was tested for sugar; then the blood vessels of both kidneys were ligated and 1 gr. of phloridzin was injected immediately. The normal blood contained 0·093 % of sugar; the blood after the operation 0·093 %.

Exp. VI. Dog, 5·7 ks. in weight. 1 gr. of phloridzin was injected after ligation of the blood vessels of both kidneys.

Sugar in the blood before the operation = 0·169 %.
,, ,, after ,, = 0·147 %.

Exp. VII. Dog, 1·374 ks. in weight. 1·5 gr. of phloridzin was injected after ligation of the blood vessels of both kidneys.

Sugar in the blood before the operation = 0·119 %.
,, ,, after ,, = 0·102 %.

The results of the experiments may be summed up in tabular form as follows:—

Percentage quantity of sugar in blood.

Exp.	Normal blood	Blood after phloridzin	Blood after ligation of renal vessels and phloridzin
I.	0·120	0·089	0·078
II.	0·170	0·109	0·121
III.	0·101	0·106	0·209
IV.	0·087	—	0·075 0·064
V.	0·093	—	0·093
VI.	0·169	—	0·147
VII.	0·119	—	0·102

Discussing these results we find that in one case after ligation of the blood vessels of the kidneys a decrease of the quantity of sugar in

the blood took place; in two other cases, an increase. This latter result coincides with that obtained by Minkowsky and seemingly corroborates his theory. But against this theory the following objections may be raised: first, that Minkowsky himself has obtained an increase of sugar beyond the normal after the extirpation of the kidneys; consequently there is not, as he claimed, simply a restoration of sugar to its normal state; and, second, that if the essence of phloridzin glycosuria actually consists in a simple elimination of sugar from the blood, we are not to expect a decrease of sugar after excluding the kidneys from the general blood circulation by the ligation of their blood vessels, and subsequent phloridzin injection. In Experiments IV—VII, however, I obtained a decrease of sugar even when the phloridzin had been injected after the ligation of the blood vessels. The tendency of the above experiments is hence against the "elimination" theory. Further the extirpation of the kidneys or the tying of their vessels is not to be regarded as an operation that leaves the other processes of the organism in their normal state. On the contrary, the changes involved were so profound that the animals survived less than two days. Evidently from the nature of the operation we have to be very cautious in drawing conclusions. Hence, the share of the kidneys in phloridzin glycosuria must be studied by other means. And it seemed to me that a comparison of the amounts of sugar in the arterial and the venous blood of the kidneys might throw light upon the "elimination" theory.

Group B.

This group comprises the results of comparison of the amounts of sugar in the blood of the renal artery and the renal vein after the administration of phloridzin.

Exp. I. Dog, 12 ks. in weight. 1·5 gr. of phloridzin was injected. On the third day afterward another injection of 0·5 gr. was made. On the fourth day cannulae were inserted into the right renal artery and the left renal vein, and blood was drawn for examination.

Amount of sugar in the arterial blood = 0·136 %.
" " " venous " = 0·143 %.

Exp. II. Dog, 10 ks. in weight. 1 gr. of phloridzin was injected. On the next day the blood of the left renal artery and right renal vein was examined.

Amount of sugar in the arterial blood = 0·150 %.
" " " venous " = 0·157 %.

Exp. III. Dog, 8·8 ks. in weight. 0·5 gr. of phloridzin was injected. On the next day the blood was taken from the left kidney only.

Amount of sugar in the arterial blood = 0·098 %.
„ „ „ venous „ = 0·121 %.

Exp. IV. Dog, 21·4 ks. in weight. 2 grs. of phloridzin were injected. During the first day he eliminated 500 c.c. of urine of sp. gr. 1050 and containing 5 % of sugar; during the second day 1000 c.c. of urine of sp. gr. 1060 and containing 5 % of sugar. On the third day the renal blood was examined.

Amount of sugar in the arterial blood = 0·118 %.
„ „ „ venous „ = 0·122 %.

Exp. V. A large dog, had been unusually long under ether. 1·5 gr. of phloridzin was injected. During the first day he eliminated 1135 c.c. of urine of sp. gr. 1020 with 4 % of sugar; on the second day 100 c.c. of urine. The renal blood was examined on the third day.

Amount of sugar in the arterial blood = 0·098 %.
„ „ „ venous „ = 0·102 %.

Exp. VI. A large dog, had been unusually long under ether. 1 gr. of phloridzin was injected. He eliminated during the day 450 c.c. of urine of sp. gr. 1060 with 4·15 % of sugar. On the second day the renal blood was examined.

Amount of sugar in the arterial blood = 0·119 %.
„ „ „ venous „ = 0·121 %.

Exp. VII. Dog, 11 ks. in weight. 1 gr. of phloridzin was injected. During the first day he eliminated 420 c.c. of urine of sp. gr. 1020 and containing 5 % of sugar. During the second day he eliminated 325 c.c. of urine of sp. gr. 1060 and containing 7 % of sugar. On the third day another injection of 0·5 gr. of phloridzin was made. During the third day he eliminated 325 c.c. of urine of sp. gr. 1070 with 10 % of sugar. On the fourth day the renal blood was examined.

Amount of sugar in the arterial blood = 0·160 %.
„ „ „ venous „ = 0·155 %.

Exp. VIII. Dog, 10 ks. in weight. 1 gr. of phloridzin was injected. In the morning of the next day another injection of 0·5 gr. of phloridzin was made. In the afternoon the renal blood was examined.

Amount of sugar in the arterial blood = 0·109 %.
„ „ „ venous „ = 0·133 %.

Exp. IX. Dog, 18·5 ks. in weight. 1 gr. of phloridzin was injected. On the next morning another injection of 0·5 gr. of phloridzin was made.

During the day the dog eliminated 350 c.c. of urine of sp. gr. 1060 with 3·3 % of sugar. The renal blood was examined on the second day.

Amount of sugar in the arterial blood = 0·127 %.

„ „ „ venous „ = 0·132 %.

The results are here grouped in tabular form:

Comparison of percentage amounts of sugar in blood of renal artery and renal vein after administration of phloridzin.

Exp.	Renal arterial blood	Renal venous blood
I.	0·136	0·143
II.	0·150	0·157
III.	0·098	0·121
IV.	0·118	0·122
V.	0·098	0·102
VI.	0·119	0·121
VII.	0·160	0·155
VIII.	0·109	0·133
IX.	0·127	0·132

The theory of von Mering and Minkowsky teaches us to expect a loss of sugar from the blood in passing through the renal circulation. In the above experiments no loss occurred except in one case (Exp. VII) and this lay within the limits of error. In Experiments III and VIII on the contrary the amount of sugar in the vein was considerably greater than that in the artery. It may be possible to explain these results by the supposition that the blood after yielding part of its water for the formation of urine leaves the kidney in a more concentrated state. But I have not noticed any relation between the amount of urine eliminated and the increase of sugar in the venous blood. The results hence speak against the "elimination" theory.

I sought next to obtain more facts concerning the activity of the kidneys in the production of sugar. To this end I considered it of value to compare the amount of sugar in the kidney itself before and after the administration of phloridzin. In two cases I extirpated one kidney, then injected phloridzin, and on the next day determined the amount of sugar in the second kidney. In other animals I ascertained the amount of sugar after the injection of phloridzin only.

Group C.

This group gives the results of comparison of the amounts of

sugar in the normal kidney and in the kidney after the injection of phloridzin.

Exp.	Wt. of dog in kilos	Amount of phloridzin injected in grs.	Normal kidney		Kidney after injection of phloridzin	
			Wt. in grs.	Percentage of sugar	Wt. in grs.	Percentage of sugar
I.	8·7	1·0	43·0	0·102	35·0	0·221
II.	13·7	1·0	45·0	0·169	41·0	0·216
III.	9·2	0·75 + 0·5	—	—	40·5	0·200
IV.	11·1	1·0 + 0·5	—	—	31·0	0·550
V.	10·2 (fasting)	1·0	—	—	42·0	0·145
VI.	15·5	1·0 + 0·5	—	—	57·0	0·281

These experiments indicate that after the injection of phloridzin the amount of sugar in the kidney may be very considerable and that it is at least greater than in the normal kidney. This latter fact indicates that in relation to the elimination of sugar the kidneys do not serve as a simple filter; it can be explained only by supposing an active production of sugar by them. This is not improbable. For they may undergo the same general nutritive changes as any other tissue of the body; and Paschutin has proved by a number of experiments that a tissue or organ may undergo carbohydrate degeneration, after its nutrition has been disturbed. Even in the brain, which in its normal state contains no carbohydrates, Paschutin found a considerable quantity of glycogen after artificial inflammation. Further, as already mentioned, Ehrlich, Straus and many others have been able to prove the presence of glycogen in the kidneys in diabetes only; and Straus failed to obtain it when he experimentally produced a hyperglycaemia. There hence appears little doubt as to the active part of the kidneys in the production of phloridzin glycosuria.

But now there arises the question, whether the kidneys are the only place of increased production of sugar during the action of phloridzin, or whether other organs play a similar rôle. Theoretically either opinion is admissible. We have just cited Paschutin's experiments by which he proves the possibility of an increased production of carbohydrates by any organ. It is evident that these carbohydrates may be eliminated in the form of sugar. There are, indeed, a great many cases of glycosuria which accompany certain local diseases. Diseased kidneys may be more prone than other organs to produce glycosuria since they

eliminate sugar more directly. But, on the other hand, we cannot deny that diseased organs may produce poisons which would disturb the metabolism of the whole body so as to result in a secretion of sugar.

As to phloridzin diabetes almost all authorities ascribe to the kidneys only, as opposed to other organs, the causation of glycosuria. And von Noorden in his latest book says: "Es ist schon erwähnt, dass der Angriffspunkt des Giftes in den Nieren zu liegen scheint, dass Phloridzin sie der Fähigkeit beraubt, die normalen Zuckermengen des Blutes zurückzuhalten. Mit dieser Erkenntniss hat der Phloridzin-Diabetes die Berechtigung verloren der Zuckerkrankheit des Menschen an die Seite gestellt zu werden." But very recently Cornevin after injection of phloridzin also found an increased secretion of sugar in the milk. Consequently in phloridzin glycosuria the kidneys are not the only sugar-forming organs.

This matter can be treated satisfactorily, however, only by a study of the sugar in all the organs together with an examination of the entire metabolism of the organism.

The general metabolism during phloridzin glycosuria has been investigated. Thus von Mering and Moritz and Prausnitz have found an increased nitrogen elimination; Quinquaud and Uschinsky do not concur in this result but find nitrogen excretion rather diminished. Furthermore, it is certain that the amount of eliminated sugar is not dependent upon either the quantity or the quality of the food. Sugar appears after continuous fasting also, when the organism is impoverished in carbohydrates.

As to the chemical analysis of the tissues but little has been done in phloridzin glycosuria. The changes of glycogen in the liver and the muscles have been investigated by von Mering and Prausnitz. Lastly, as we have seen, investigations of sugar in blood have been made after the injection of phloridzin only (von Mering), after phloridzin injection and ligation of the ureters or blood vessels of the kidneys (Uschinsky), and after phloridzin injection and extirpation of the kidneys (Minkowsky). As already mentioned, von Mering after three determinations of the sugar in the blood propounded his "elimination" theory.

In order to ascertain whether phloridzin glycosuria derives its sugar simply by impoverishing the blood, or whether more profound changes take place in the tissues, I undertook some analyses of the blood. I examined the amounts of water, solids, sugar, proteids, ethereal extract containing fat, cholesterin, and lecithin.

Group D.

This group contains the results of analysis of the blood of dogs before and after the administration of phloridzin.

Exp. I. A dog, 9·8 ks. in weight, was fed daily for some days before and during the experiment with 250 grs. of meat free from fat. Some blood was taken from the carotid artery and analyzed; 1 gr. of phloridzin was then injected. On the next day another injection of 0·5 gr. of phloridzin was made. On the fourth day the blood was again examined.

The results of the analyses are shown in the following table:

	Before injection of phloridzin	After injection of phloridzin
Water	76·0 %	79·9 %
Solids	24·0 „	20·1 „
Glucose	0·161 „	0·143 „
Proteids	23·3 „	18·8 „
Serum albumen	21·0 „	15·4 „
Serum globulin	2·3 „	3·4 „
Fat, cholesterin and lecithin	0·27 „	0·33 „

Exp. II. A dog, 18 ks. in weight, received on the days before and after the first examination of blood 400 grs. of meat. After an examination of the blood 1·5 gr. of phloridzin was injected. On the next day 0·5 gr. of phloridzin was injected. On the third day the blood was again examined. The results of the analyses are as follows:

	Before injection of phloridzin	After injection of phloridzin
Water	78·6 %	78·6 %
Solids	21·4 „	21·4 „
Glucose	0·117 „	0·113 „
Proteids	21·0 „	20·0 „
Serum albumen	16·0 „	14·5 „
Serum globulin	4·8 „	5·5 „
Fat, cholesterin and lecithin	0·31 „	0·35 „

Exp. III. A dog, 21·4 ks. in weight, received about 800 grs. of meat on the days before and after the examination of the blood. After the first examination of the blood 2 grs. of phloridzin were injected. On the third day a second examination of the blood was made. The results of analyses are as follows:

	Before injection of phloridzin	After injection of phloridzin
Glucose	0·114 %	0·121 %
Proteids	21·3 „	20·8 „
Serum albumen	16·95 „	13·0 „
Serum globulin	4·35 „	7·8 „
Fat, cholesterin and lecithin	0·4 „	0·3 „

Exp. IV. A dog, 16·5 ks. in weight, received before the examination 280 grs. of meat. After the first examination of the blood 1·5 gr. of phloridzin was injected. On the next day the dog received 120 grs. of meat; on the third day 250 grs. Here are the results:

	Before injection of phloridzin	1 day after injection of phloridzin	2 days after injection of phloridzin
Glucose	0·210 %	0·131 %	0·223 %
Proteids	22·0 „	16·6 „	19·5 „
Fat, cholesterin and lecithin	0·36 „	0·39 „	0·36 „

Exp. V. A dog, 10·6 ks. in weight, fasted two days before and during the experiment. After the first examination of the blood 1·5 gr. of phloridzin was injected. Here are the results:

	Before injection of phloridzin	1 day after injection of phloridzin	2 days after injection of phloridzin
Glucose	0·150 %	0·114 %	0·150 %
Proteids	22·85 „	19·3 „	—
Fat, cholesterin and lecithin	0·29 „	0·33 „	—

Summing up the results of the above experiments and comparing them with those found for spontaneous diabetes, we find by experiment with phloridzin almost a constant decrease of the general amount of proteids and a varied relation between the serum albumen and the serum globulin. Serum albumen is usually decreased in quantity; serum globulin increased. These results are important inasmuch as they tend to show increased decomposition of the proteids in the body. This relation is also observed in fasting. The possibility of fasting in the above cases is excluded, however, by the fact of food having been given to the animals throughout the experiment, except in No. V.

The ethereal extract containing fat, cholesterin, and lecithin is in most cases increased, which again agrees with spontaneous diabetes (Jaksch, Gamgee).

As to the substance most essential to diabetes, the sugar, I have, like others, frequently found some decrease of it in the blood. But this is

by no means constant; and there are also cases of increase of sugar. (See Exps. III and IV.) It is also true that the fluctuation of the amount of sugar in either direction, is in most cases very slight. In my opinion it is difficult to explain phloridzin glycosuria by hyperglycaemia, as it is difficult to explain it by the mere extraction of the sugar from the blood. Such explanations are all the more improbable since the decrease of sugar in the blood is not proportional to the quantity of the sugar eliminated by the urine, as we might have expected, if we accepted the "elimination" theory. On the other hand we do frequently observe that a relatively higher amount of sugar in the blood is accompanied by its increased elimination in the urine. But increased glycaemia is not a necessary concomitant of spontaneous diabetes. "Es ist nicht richtig dass die gesteigerte Glykaemie eine nothwendige Bedingung für die Glycosurie ist," says Seegen. This opinion he bases upon an examination of a considerable number of patients suffering with diabetes, whose blood did not contain an amount of sugar above the normal. Consequently in this respect phloridzin glycosuria does not differ from what is observed in *diabetes mellitus*.

Thus the general analysis of the blood seems to show that phloridzin glycosuria does not originate simply in the extraction of sugar from the blood, but that more profound changes in the tissues take place, and that these changes corroborate the views of those authors who see the source of sugar in phloridzin glycosuria in the decomposition of proteids. The absence of hyperglycaemia may be explained by the supposition that the organism has not lost its ability to rid itself of the superabundance of sugar; on the one hand by its elimination through the kidneys, and, on the other, by its increased decomposition. In favour of the latter supposition may also be construed the increased quantity of the ethereal extract, which may be regarded as possibly the product of the decomposition of sugar; and also the fact that the decrease of sugar sometimes takes place even when phloridzin is injected after the ligation of the renal blood vessels. It may also be observed that if phloridzin glycosuria represented simply the decrease of sugar in the organism, it would present symptoms characteristic of carbohydrate inanition only and it would be difficult to explain the rest of its symptoms.

Conclusions.

Thus we are confronted with two views on the origin of phloridzin diabetes. Some think it the result of a simple elimination of sugar

from the organism by the kidneys; others see in it an excessive formation of glucose.

The first base their view on the slight decrease of sugar in the blood after the injection of phloridzin and on the fact that after the extirpation of the kidneys the quantity of sugar in the blood is somewhat increased in some cases. But no one has succeeded in establishing a fixed relation between the quantity of sugar in the blood and the sugar eliminated. Furthermore I have obtained a decrease of sugar in the blood in some cases when the phloridzin was injected after ligation of the renal vessels. Finally, as demonstrated by Cornevin, the phloridzin greatly increases the quantity of sugar eliminated by the milk. Consequently this poison does not affect the kidneys only. The operation of extirpation of the kidneys can scarcely be considered as decisive of the question of the origin of the glycosuria.

As to the second view, that there is an increased production of sugar, and that more especially by the kidneys, I may contribute the facts that the venous blood of the kidneys in phloridzin glycosuria contains in some cases more sugar than the arterial, and that the quantity of sugar in the kidney tissue itself increases after the injection of phloridzin.

Finally, the composition of the blood in phloridzin diabetes testifies to the decomposition of proteids rather than to the mere elimination of sugar.

I deem it a pleasant duty to express my thanks to Prof. J. G. Curtis and Dr. F. S. Lee for the privilege of their laboratory and for the help extended to me during my work.

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P. A. Levene.

Studies from The Department of Physiology of Columbia College at the College of Physicians and Surgeons. Vol. I.

[Reprinted from the New York Medical Journal for June 15, 1895.]

AN EXPERIMENTAL STUDY OF DIRECT AND INDIRECT FARADIZATION OF THE DIGESTIVE CANAL

IN DOGS, CATS, AND RABBITS.*

By S. J. MELTZER, M. D.,

NEW YORK.

The electrization of the stomach or the intestines has for its purpose, among other things, the production of contraction in these organs. As is well known, two methods are at present employed in the electrical treatment of the digestive canal: the *percutaneous* and the *direct* electrization. In the percutaneous electrization both electrodes are placed outside, on the abdominal wall, in a manner which is deemed best to reach the organ in view. In the direct electrization one electrode is applied to a selected place on the abdominal wall, and the other electrode is introduced either into the rectum or into the stomach. Both methods are extensively employed by neurologists, and by the specialists for the stomach, as well as by the general practitioners. The application of electricity by these methods presupposes that the current reaches the muscular coat of the stomach or of the intestines, and reaches it in such a strength as to produce a local contraction which is then the cause of a peristaltic movement of either the stomach or the intestines. In the extensive literature on our subject we meet hardly a dissenting voice as to the correctness of this supposition. The statements that the electrization of

* Read before the Association of American Physicians at its tenth annual meeting.

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the abdomen is sometimes followed by defecation; von Ziemssen's * statement of the visible or palpable contraction of the intestines in a hernia during its electrization; the quicker disappearance of water from the stomach or the earlier appearance of the salol test after the electrization of the stomach; these are the main clinical proofs for the effectiveness of the electrization upon the motor part of the digestive canal. In a case of cancer of the pylorus with visible peristaltic waves of the dilated stomach, Pepper,† however, reported that the percutaneous electrization of the stomach did not influence its visible peristalsis. Kussmaul,‡ on the other hand, states that he has seen in one case the visible peristaltic waves on a dilated stomach quickened by the direct (internal) electrization. This seems to speak in favor of the direct and against the percutaneous electrization. Indeed, all writers seem to agree that the direct electrization is preferable to the subcutaneous application. The objection against the former is based mainly upon its inconvenience for the patient; but since the introduction of improved stomach electrodes (Einhorn's # deglutable electrode; Ewald's‖ modification of it; Wegele's△ spiral electrode) the inconvenience has been considerably reduced. It seems to be in harmony with the general sentiment at present when Ewald thus says: "Surely, by using Einhorn's stomach electrode or my modification of it, contractions of the muscular fibres of the stomach themselves must be obtained." Ewald,◊ however, says also: "It must, unfortunately, be admitted that all such therapeutic procedures which may be complicated by other factors, do not of themselves prove much until we have the ocular proof of seeing the stomach contract under the influence of the electric current." This "ocular proof of seeing the stomach contract" is, as far as I have been able to see, not yet fur-

* Von Ziemssen. *Die Electricität in der Medizin*, 4. Aufl., 1892.

† Pepper. *A Case of Scirrhus of the Pylorus, with Remarks on the Electrical Excitation of the Stomach.*

‡ Kussmaul. *Archiv für Psychiatrie*, Bd. viii.

Einhorn. *Med. Record*, May 9, 1891.

‖ Ewald, C. A. *Berliner klin. Wochenschrift*, 1892, No. 26.

△ Wegele. *Therapeutische Monatshefte*, April, 1895.

◊ Ewald, C. A. *Diseases of the Stomach.* Translated by Manges, 1892, p. 68.

nished. The present status is then as follows: It is a generally prevailing view that the percutaneous electrization of the stomach and intestines produces a contraction of these organs; it seems to be universally accepted that stimulation of the mucous membrane of the stomach is the most direct and safest way to effect its contraction. There is no positive proof of either of these assumptions.

While studying the influence of the vagus upon the stomach, I made an unexpected observation which gave rise to a series of experiments upon animals bearing upon the subject of electrization of the stomach and intestines. The results of these experiments I am now going to report.

The electricity in my experiments has reference only to the faradaic current. I employed the large sliding *inductorium* of Du Bois-Reymond with more than ten thousand coils; the primary coil was connected with a Grove's cell, freshly arranged for each experiment, while the secondary coil formed with a Du Bois-Reymond key a closed circuit As is well known, the strength of the current in such an apparatus is measured by the distance between the secondary and primary coils. In my report I shall term it briefly the *distance*. The current is increased with the shorter distance, but not in exact proportion, the increase of the current occurring more rapidly the nearer the secondary coil comes to the primary. For instance, the increase of the current is greater when the secondary coil is moved from one hundred to ninety than when moved from two hundred to a hundred and ninety millimetres distance.

All the animals were under thorough anæsthesia: chloral for the rabbits and ether for the dogs and cats; in a few cases the animals were also under the influence of curare. Artificial respiration was employed in nearly all the experiments. The results obtained were verified in all the three kinds of animals; the greatest number of experiments, however, were made on dogs, which are best suited for our purpose. The stomach of the rabbit is not a good object for studying the main phenomenon of our results. The stomach of the cat, on the other hand, is rather a good object for study, but this animal succumbs quickly to the influence of ether, and is therefore harder to handle. I am not going to bother you with a detailed account of all my

experiments; I shall only report the results which were derived in each case, not from a single but rather from an oft-repeated experiment, giving a uniform effect.

Experiments on the Stomach.—The abdomen of a dog is opened, the omentum is removed, and the entire stomach is exposed to a full view and kept constantly moist with a physiological saline solution. For local stimulation two copper wires were employed which were conveniently united in a well-polished wooden handle; the wires were flattened at the end and stood about one centimetre apart. By successively stimulating with this double electrode the entire surface of the stomach, it was established that only about one third of it responded with a distinct contraction to an efficient local stimulation. A line drawn perpendicularly from the middle of the cardia to the large curvature divides the stomach into two parts. The part lying to the right of the line is contractible, and the remaining part, or we might say the fundus, is nearly incontractible: a strong and long stimulation produces a hardly perceptible effect. The contractibility of the cardio-pyloric part seems to be the better the nearer we come to the pylorus. The change in the contractibility of the two parts occurs quite abruptly. Exactly the same conditions we meet with in the stomach of the rabbit; the very large fundus of this animal is quite incontractible. In cats, however, an efficient stimulation produces a well-marked local contraction in all parts of the stomach, which by the way, does not have a well-developed fundus and is altogether correspondingly smaller than in the other two animals. If there has not been any peristalsis going on before electrization, a local stimulation effects only a local contraction, except in the pylorus, where a stimulation brings on a wavelike contraction of this entire part. If there were peristaltic movements going on in the cardio-pyloric part before the stimulation was started, then a local contraction was sometimes the cause of spreading a new peristaltic wave over the contractible area.

If we select a place on the stomach which is capable of giving us a well-marked contraction, and then look for the strength of the current which is capable of calling forth such a contraction, we find that the first signs of a con-

traction become noticeable at a distance of two hundred to a hundred and eighty millimetres, and get more and more pronounced as we are gradually moving forward the secondary coil, until at about a hundred and thirty millimetres distance we obtain the maximum effect. Such a maximal contraction appears like a deep groove on the stomach, which stands parallel to the vertical axis of the organ. The contracted part looks pale and ischæmic, and reminds one of an old scar from a burn. If a strong stimulus is used, the latent period is quite short, and the contraction lasts for more than twenty seconds after the stimulation was interrupted. Of course, the numbers mentioned vary to a certain degree; but I do not recall any case where a still shorter distance than a hundred and twenty millimetres was required to obtain a maximal contraction.

After determining such a well-contracting place, an opening was made in the fundus, the contents of the stomach were removed, and the mucous membrane was cleansed with a saline solution. I then introduced the double electrode into the cavity of the stomach, applying its ends to the mucous membrane right opposite the determined place on the outer surface. When I now opened the key while the distance of the secondary coil was still the same as it was when used for the maximal contraction, not the slightest contraction could be noticed even after prolonged stimulation! The immediate stimulation of the outer surface produces the usual contraction—the effect did not suffer by the opening and cleansing of the stomach. As long as the heart continues to beat and the stomach is kept sufficiently moist, the experiment can be repeated again and again with uniformly the same result. The stimulation of the mucous membrane remains without any effect, even when the strength of the current is considerably increased; the secondary coil can be shifted forward to a hundred and ten, to a hundred, or to ninety millimetres distance, or even still nearer to the primary coil, without a sign of a contraction making its appearance. This, however, is not absolute. A very strong current will finally penetrate the stomach wall. At a distance of forty or fifty, sometimes already at eighty or even ninety millimetres the stimulation of the mucous membrane does not fail to pro-

duce a well-defined contraction. Usually the current is then exceedingly strong; but even then the effected contraction is in no comparison to those contractions obtained by stimulation of the outer surface with a distance only of a hundred and thirty to a hundred and forty millimetres. In fact, even at zero the contraction produced from the mucous membrane is much weaker than the maximal contraction from the outer surface. The same remarkable difference we find also to exist in the stimulations of both surfaces of the stomachs of the cats and rabbits. The stomach of the latter animal, however, is usually overfilled and very distended; when it is emptied it shrinks considerably and it appears to be in a contracted state. The difference can be clearly seen even then, but the stomach is in this state by no means a good object for our study. Furthermore, I found the difference under discussion to exist also in the stomach of the frog; but this thick walled stomach, with its small and slow contractions, was certainly not a desirable object for an extensive study of our phenomenon. I wish to add that in studying the effect of a stimulation it is necessary to be aware of the accidentally passing by of a peristaltic movement which might be mistaken for a local contraction.

To decide the question whether in electrizing the mucous membrane any current at all is passing through the stomach wall, I made the following experiment: The sciatic nerve of the animal was placed in a Ludwig's nerve electrode, the protruding wires of which were connected by means of flexible conductors with another pair of electrodes. These latter, being only a few millimetres distant from one another, were placed on the outer surface of the stomach, just opposite the space between the electrodes adjusted to the mucous membrane. When, now, the current leading to the latter electrodes was closed the leg of the animal began to jerk. That certainly means that the current passed through the wall of the stomach, and then by the way of the outer electrodes through the sciatic nerve. I made use of this practical arrangement also for some other purposes. For brevity's sake, I shall hereafter refer to this arrangement as the sciatic electrodes. When I connected the outer electrodes with the uncovered abdom-

inal muscles instead of with the sciatic nerve, the closure of the current did not produce a contraction of these muscles. All this goes to show that a current does pass through the wall of the stomach of sufficient strength to stimulate a motor nerve, but not strong enough to stimulate skeletal muscles, and certainly not strong enough to produce even a minimal contraction of the unstriated muscular tissue of the stomach.

My next line of experiments was to study the effect of electrical stimulation upon the stomach when one electrode was introduced into the stomach and the other applied to its outer surface. For these experiments the animals did not receive any food for two days previous to the experiment. In dogs the stomach was then usually sufficiently empty. The stomach electrode had a thickness of a few millimetres; its connecting wire was hidden within a stomach tube open at the end. It is worth mentioning that after introducing the electrode through the mouth into the stomach, it was always found to be located in the fundus, just outside of the contractible part of the stomach. By bending the wire to the right side I succeeded in placing the protruding point of the electrode into the middle of the contractible area. As an outside electrode I used a metal ball of about fifteen millimetres in diameter attached to a wooden handle. The results of these experiments were uniformly as follows:

When one electrode was introduced through the mouth into the stomach and the other placed on the outer surface of it, about two centimetres or more away from the protruding internal electrode, there was no contraction to be seen even with a strong current; but if both electrodes were placed very near one another, a strong current produced a contraction which was the stronger the nearer both points of the electrodes were to one another. If a piece of omentum, however, was placed between the stomach and the outer electrode, the current produced no effect even when both points of the electrodes stood one just over the other. I should add here that the presence of omentum on the stomach did not impair the effect of the stimulation in the case when both electrodes were placed on the outer surface. If the internal electrode was not pressed well

against the wall of the stomach, but was suspended within the cavity, which was filled for this purpose with a saline solution, no contraction could be effected, no matter where the outer electrode was placed.

To test still more definitely the value of the direct electrization of the stomach as it is employed clinically, the following experiments were made:

1. The internal electrode was either immersed in the saline solution within the cavity of the stomach or pressed distinctly against the wall of the contractible part of the stomach; this part was then put in such a position as to be easily accessible to the view. The external electrode, the one used before, or a large sponge was placed upon the well-shaved abdominal wall in the nearest neighborhood of the stomach. A strong current produced a strong contraction of the abdominal muscles, while the stomach remained perfectly motionless. This shows that the contraction of the abdominal muscles beneath the outer electrode is by no means a proof that the stomach is also contracting. In connection with this I wish to register the observation that by means of the sciatic electrode I could prove the presence of a current in a large area around the external electrode, while the area around the internal electrode, from where the sciatic nerve could be stimulated, was certainly not more than two centimetres in diameter. Against this experiment it could perhaps be said that the direct line between the two electrodes was longer than in the usual direct electrization, and it led perhaps through the incontractible part of the stomach.

2. The wound above the stomach was tightly stitched together, but so as to be able to be opened again in a second or two; the blood at the edges of the wound, which could possibly serve as a direct conductor, was well removed. While the internal electrode was pressing against the front wall of the stomach, the external electrode was put upon the wound, so as to be in the shortest line to the contractible part of the stomach and the internal electrode. A strong current produced a contraction of the abdominal muscles. After interruption of the current the wound was hurriedly opened, the procedure not lasting longer than two seconds; the stomach was then found in the same re-

laxed condition as before. Whereas we know that a well-defined local contraction of the stomach lasts about twenty seconds after interruption of the stimulation, we must concede that the electrization did not produce a contraction of the stomach. But here again it might be asserted that there was a weak contraction with only a short after-effect which disappeared before the wound could be opened.

3. The electrodes connected with the sciatic electrode were placed upon the stomach just above the internal electrode and covered with omentum; the wound was then well sutured in its entire length, except a small opening at its lower end. The external electrode was then placed on the abdominal wall in the closest proximity to the electrodes on the stomach, and the current was turned on: no motion of the leg, even when the secondary coil was put at zero! This certainly shows unmistakably that when one electrode is placed within the stomach and another electrode placed on the skin just above the stomach, there is on the surface of the stomach, even with the strongest faradization, no current strong enough to stimulate a motor nerve, and certainly not strong enough to produce even a slight contraction of the stomach!

By the last three experimental methods I was enabled to test also the value of the percutaneous faradization of the stomach, and I shall state their results briefly. The corresponding places of the abdomen were shaved and sponge electrodes were applied, one in the back (Erb) and one in the front in the manner soon to be stated. When the stomach was exposed to view and the electrode set upon the skin nearest to the stomach, the abdominal muscles and the muscles in the back were contracting, but not the stomach. When the wound was stitched, an electrode applied on it and stimulated, the abdominal muscles contracted, but a quick reopening of the abdomen did not reveal a trace of contraction of the stomach. When, finally, the sciatic electrode was applied on the stomach, the wound sutured, and the external electrode placed just above the other electrodes, no current, ever so strong, produced a contraction of the limb.

Thus my experiments demonstrated definitely that neither the percutaneous nor the so-called direct faradization

of the stomach was capable of producing a contraction of the stomach, at least in the animals I experimented upon.

The Experiments on the Intestines.—My experiments on the intestines are in most respects a repetition of the experiments upon the stomach, and will be reported briefly.

As is well known, the direct application of both electrodes on the intestines produces a strong constriction of the stimulated part, including a few millimetres outside of each electrode. This local contraction is very rarely the cause of an extended peristalsis. The contraction overlasts the stimulation for fifteen to twenty seconds. The local contraction of the intestines can be effected with a much weaker current than the one required for a well-defined contraction of the stomach. The current which is just sufficient to produce a strong local contraction of the intestines by stimulating their outer surface will produce no contraction by the application of the electrodes to the mucous membrane. This holds good only in dogs. In rabbits I find that an effective current for the outer surface seems to be effective also for the internal surface, except that the contraction is considerably weaker, and even in dogs a slight increase in the intensity of the current will suffice to call forth a contraction by faradization of the mucous membrane. But I can not recall ever having seen one of these contractions being remotely so strong as the ones which can easily be effected by stimulating the outer surface. And there is another difference between the conditions of the intestines and those of the stomach. If one electrode is placed on the outer surface of some part of the intestine and the other electrode is applied to the mucous membrane of even a distant part, there will always be a contraction of the part where the outer electrode rests. Furthermore, the same result will be obtained if the inner electrode is placed in the rectum or in the stomach. On the other hand, the stomach will contract if one electrode is placed upon its outer surface and the other electrode is placed within some parts of the intestines or inserted into the rectum, while it does not contract, as stated above, if this (inner) electrode is placed in the cavity of the stomach itself! If one electrode is placed within the stomach and the other in the rectum, be both cavities

cleansed or not, there will be no contraction in any part of the digestive canal. This latter experiment was done already by Schillbach,* who reported that he had seen no results from this mode of electrization. Ewald,† who distrusts this statement, attributed the negative result to the unclean state of both cavities. Apparently Ewald thought that there was no current at all. This, however, is not so. Even when these cavities are not cleansed an effective current is present, as can be seen by the tetanic contraction of the lower extremities, or by the sciatic electrodes applied to any part of the abdominal viscera lying between the stomach and the rectum, only that the intestines, rectum, and stomach remain motionless. In this respect, however, the result is not altered even by a scrupulous cleansing of the employed cavities.

Concerning the effect of the electrization of the intestines by the application of both electrodes percutaneously, or one electrode in the rectum and the other on the abdominal wall, I will say briefly that the result was exactly the same as in the electrization of the stomach; the intestines remain unaffected by the current. I arrived at this conclusion by the same method which I employed for the test of the value of electrization of the stomach, as described above in full, and which I shall now point out briefly: By ocular observation, by closing and reopening the wound, and by the sciatic electrodes.

I shall add that the results of my experiments represent only the rule and do certainly not exclude the possibility of exceptions—that means that under certain very favorable conditions a current might indeed reach some parts of the abdominal viscera even by percutaneous faradization. As such an exception I am inclined to consider the above-quoted observation of Kussmaul respecting the increase of the peristalsis by electrization, and perhaps the much-quoted case of von Basch ‡ is another such exception. Of this latter case I should like to speak here a little more in detail. An emaciated woman, whose thin abdominal wall von Basch was electrizing for a few minutes with a very strong current,

* Schillbach. Virchow's *Archiv*, Bd. cix, p. 284.

† Ewald. *Diseases of the Stomach*, *loc. cit.*

‡ Von Basch. *Wiener med. Blätter*, 1878, No. 12.

fell suddenly into a dangerous faint, from which she recovered after her abdomen was massaged. Von Basch explained this accident by the supposition that the electrization produced hyperæmia of the abdominal viscera, which in turn brought on a cerebral anæmia, and this latter was the cause of the syncope. He adds, however, that the fainting spell could also be explained by a reflex action from the viscera upon the vagi. The case in itself is certainly not a strong one. An emaciated woman can be made to fall in a faint by any sort of unusual instrumental manipulations with her. My interest in this case, however, comes from observations I have made on animals. While electrizing the intestines of a dog, by having one electrode in the rectum and the other on the intestines, I noticed that the intestines became paler and paler, until they were nearly white. Upon examining the heart I found that it had stopped beating. The dog, which was living three minutes before, was dead. Later on I was careful to discontinue the faradization as soon as I noticed that a change in the color of the intestines was taking place. My explanation of this occurrence is that the current struck the splanchnic nerves, and thus produced on the one hand anæmia of the intestines by the stimulation of their vaso constrictor nerve fibres contained in these nerves, and on the other hand a standstill of the heart by the well-known reflex from the viscera through the splanchnics and sympathetic to the vagi (Goltz's *Klopfversuch*). I also observed that the stimulation of the intestines sometimes effected a standstill of the respiration, at least in rabbits with natural breathing. This means also an inhibitory reflex action carried by the splanchnics to the respiratory centre (Graham). Now, if the syncope in the case of von Basch was indeed due to the current reaching the intestines, I would then believe that the intestines were not in a state of hyperæmia, as von Basch puts it, but rather in a state of anæmia, the entire accident being similar to my experience with the dog. Accordingly, we may state that by some exceptionally favorable facilities a current coming from the electrization of the abdominal wall might indeed reach the intestines. But then we should bear in mind that it might occasionally have a fatal effect.

Before concluding, I have to add a few remarks with reference to the electrization of mucous membranes. Faradization of the mucous membrane of the pharynx or of the tongue produces a contraction of the muscles beneath them exactly as if there were no membranes between the muscles and electrodes. In faradization of the mucous membrane of the œsophagus in its upper third the effect is like directly electrizing striated muscle tissue—the contraction sets in with the closure and disappears with the opening of the circuit. In the few instances in which I have tried it, I have found that with the internal electrization the circular contraction, and with the external the longitudinal contraction, predominates. On the behavior of the mucous membranes of the stomach and the intestines I have reported above. There is not much difference between the small and the large intestine, but there is a marked difference between them and the rectum; here the mucous membrane is nearly as responsive as the outer surface. There is also in the bladder a pronounced difference between the effects of stimulation of the mucous membrane and those of stimulation of the external surface. In the non-gravid uterus I have not been able to produce any contraction, and a gravid one has not been at my disposal.

The general feature of these experiences is that those mucous membranes which cover striated muscular tissue form no obstacle to the current, and those which cover plain muscular tissue do form an obstacle; within this latter class, again, the tissue which is least irritable is covered with a mucous membrane which offers the greatest resistance to the electrical current. Thus, the muscular coat of the stomach is the least excitable and the mucous membrane offers the greatest resistance. That the difference in the excitability of the muscular tissue is not the only cause for the proved resistance of the mucous membrane of the stomach or intestines can be proved by the following experiment: The mucous membrane of the tongue is replaced by a piece of mucous membrane of the stomach; faradization now does not produce a contraction of the muscles of the tongue. That is also the meaning of the above-quoted experiment—*i. e.*, that electrodes placed upon the outer surface of the stomach could transmit an effective stimulus to

skeletal muscles by the way of the motor nerve, but not by direct application of muscular tissue. We can now understand the meaning of some of the apparently paradoxical experiments on the stomach and intestines. The muscular coat of the stomach is less irritable than the coat of the intestines, and the mucous membrane of the stomach offers a greater resistance than that of the intestines. Therefore, if one electrode rests upon the mucous membrane of the intestines and the other upon the muscular coat of the stomach, the latter contracts because the mucous membrane in point has a smaller resistance, or, if one electrode rests upon the mucous membrane of the stomach and the other upon the muscular coat of the intestines, the latter contracts on account of the greater excitability of this muscular tissue. But if one electrode is upon the mucous membrane of the stomach and another rests upon its muscular coat, then there is no contraction, because the muscular tissue in question is the least excitable and the mucous membrane offers the greatest resistance. What the resistance means, what are its nature and extent, I should not attempt to answer for the present; it is reserved for a further study.

The main results of my experiments are, then, briefly stated as follows:

The mucous membrane of the digestive canal offers a considerable resistance to the penetration of the faradaic current to the muscular coat; the greatest resistance is found in the mucous membrane of the stomach.

The percutaneous and the direct faradization of the stomach or the intestines can not produce any contraction in these parts.

My statements have reference only to the animals I experimented with. However, abdominal surgery might offer an opportunity to test their validity for the human being.

[*Studies from the Physiological Laboratory of the College of Physicians and Surgeons, Columbia University, New York City, vol. i.*]

ON ABSORPTION OF STRYCHNINE AND HYDROCYANIC ACID FROM THE MUCOUS MEMBRANE OF THE STOMACH.—AN EXPERIMENTAL STUDY ON RABBITS.*

By S. J. MELTZER, M. D.

It has always been, and still seems to be, the prevailing opinion that the stomach is capable of absorbing soluble and diffusible substances, and there seemed, indeed, to be no reason to suppose that the mucous membrane of the stomach should with regard to absorption be inferior to any other mucous membrane.

Recent investigations, however, have brought to light some new facts with regard to the power of absorption of the stomach, the most striking of which is surely the unexpected result that the stomach does not absorb any water. Edkins† introduced into the stomach of cats, after the ligation of cardia and pylorus, a measured quantity of salt solution, and recovered after an hour exactly the same quantity again. Von Mering,‡ who experimented on dogs with a duodenal fistula, found that a larger quantity of water came out through the fistula than the dogs had taken by the mouth. As my experiments have reference mainly to the absorption of strychnine and of hydrocyanic acid, I shall restrict my references to literature to those having direct bearing upon this subject. As far as I can ascertain,

* Read at the Eleventh Annual Meeting of the Association of American Physicians, April 30, 1896.

† J. S. Edkins, The Absorption of Water in the Alimentary Canal. *Journal of Physiology*, 1892, p. 460.

‡ Von Mering, Ueber die Functionen des Magens. *Therapeutische Monatshefte*, Mai, 1893.

Reprinted from The Journal of Experimental Medicine, vol. i, No. 3.
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there are only two statements on the absorption of strychnine in the stomach.

Bouley and Colin * have introduced strychnine into the stomach of animals whose pylorus was either ligated or paralyzed by vagotomy. They report that in the dog, swine, and cat the effects of the strychnine appeared very rapidly; the effect was retarded in the cow, and there was no effect—at least, no fatal effect—in the horse. Tappeiner † has experimented with strychnine exclusively upon cats, in whose stomach the poison was introduced through a stomach tube. A normal cat of about 2 kilos succumbed to the effects of 0.03 gramme of strychnine in an aqueous solution in eight minutes; cats whose pylorus was tied succumbed to doses of 0.05 and more only after an hour and thirty minutes or even later. If the strychnine solution, however, contained some alcohol, the strychnine took effect almost as rapidly as when the pylorus was not tied. Tappeiner also found that chloral hydrate in aqueous solution was not absorbed in the stomach of a dog with closed pylorus, while an alcoholic solution of it was readily absorbed.

Concerning the absorption of prussic acid from the stomach, I could find no reference.

My experiments relate to the absorption of various solutions in dogs and rabbits, and also in frogs, but I shall report here only the results I obtained in rabbits with strychnine nitrate and hydrocyanic acid. The animals were all well narcotized with ether during the operation. In most cases, after the introduction of the poison into the stomach, the pyloric and cardiac ends of the stomach were tied. At the pylorus the ligature was applied in the groove between the pylorus and duodenum, avoiding the inclusion of the vessels of the stomach, and at the cardia the ligature was applied on the œsophagus just beneath the diaphragm. I shall now let the experiments speak for themselves.

Experiment 3.—Rabbit, 1,800 grammes, not starved. Through a soft catheter, introduced by the mouth into the stomach, 10 milli-

* Colin, Traité de physiologie comparée, vol. ii, p. 91.

† Tappeiner, Ueber Resorption im Magen. *Zeitschrift für Biologie*, 1880.

grammes of strychnine were injected, catheter removed, and rabbit taken off from the board. After fourteen minutes a typical strong tetanus broke out; a few more followed, and the rabbit died.

Exp. 41.—Rabbit, 1,760 grammes, not starved. Through an opening made in the œsophagus a catheter was introduced into the stomach, and 6 milligrammes of strychnine in water coloured with methylene blue injected. Rabbit put on a box. After eighteen minutes, animal showed great uneasiness, and nine minutes later, with a sudden jerk, a strong opisthotonos set in, which lasted over two minutes. Rabbit remained hyperæsthetic for half an hour, and gradually recovered.

These two control experiments are sufficient to show that 6 to 10 milligrammes of strychnine brought into the full stomach of a rabbit do not fail to produce within half an hour the characteristic effect.

Exp. 4.—Rabbit, 980 grammes, starved three days, stomach nearly empty. Cardia tied, an opening made in duodenum, and a thin catheter introduced into the stomach, reaching the wall of the fundus. Sixty milligrammes of strychnine in 10 cubic centimetres of a forty-per-cent alcoholic solution, coloured with indigo carmine, were injected, the tube removed, duodenum and abdomen sewed up, and the animal brought to the box. The rabbit lived fifteen hours, and at no time was there any sign of hyperæsthesia, of increased reflex irritability, not to speak of a convulsion. The death was apparently due to peritonitis and aspiration pneumonia ("Schluckpneumonie"), but certainly not to strychnine poisoning. The stomach was considerably distended, and apparently contained more fluid than before the ligation.

It might be claimed that the explanation of the striking fact that 60 milligrammes of strychnine could remain for fifteen hours in the stomach without absorption is that by the ligation of the cardia and pylorus all the blood vessels and the lymphatics of the stomach were ligated, thus leaving no path open by which the poison could have been carried into the circulation. However, the stomach had by no means an ischæmic appearance; on the contrary, distinct pulsation could be seen also after the ligation, and the stomach retained in every respect its natural appearance. At any rate, such a claim can not be raised against the following experiment.

Exp. 7.—Middle-sized rabbit, pylorus ligated, cardia open; introduced through a catheter by the mouth 60 milligrammes of strychnine

in an aqueous solution. Rabbit lived nineteen hours without showing any effects of strychnine. Death and autopsy as in the preceding experiment.

Here the vessels of the cardiac end of the stomach remained open; nevertheless no absorption took place.

Exp. 28.—Rabbit, 1,200 grammes, starved two days, cardia left open; introduced a tube through the duodenum into the stomach; injected into the fundus 45 milligrammes of strychnine; rabbit remained for an hour on the holder; no sign of any effect. Then the rectum was tied, and by a hypodermic syringe 3½ milligrammes of strychnine, coloured with indigo carmine, were injected through the wall of the rectum into the impacted lumen. After twelve minutes a tetanic outbreak set in, which terminated fatally. The tetanic outbreak was apparently due to the quick absorption of the 3½ milligrammes of strychnine from the rectum. No drop escaped into the peritoneal cavity or infiltrated the wall of the rectum, as could be seen by the absence of the blue colour.

Against the conclusion that the mucous membrane of the stomach of the rabbit does not absorb strychnine, another objection could be raised, namely, that the stomach of the rabbit is never thoroughly empty, and that the strychnine in all the cases is enveloped by the remnants of the food and does not come in contact with the mucous membrane at all. To meet this objection, the following experiment was made:

Exp. 35.—Rabbit, 1,200 grammes, starved sixty hours, stomach quite empty. By a catheter, which was introduced through an opening in the œsophagus, 100 cubic centimetres of water were brought into the stomach, catheter removed, and cardia left open. A tube was introduced through duodenum and pylorus; the inner end of this tube was brought in close proximity with the wall of the stomach, then 60 milligrammes of strychnine, deeply coloured with indigo carmine, was injected, and some air blown in; now the tube was removed and the pylorus tied. An hour and twenty minutes passed by without a sign of a strychnine effect. Judging from the manifold experiences I had had I was sure that if the rabbit did not show the effects of the strychnine in the first hour the effect would not appear at all. Therefore the rabbit was used for another experiment. Three milligrammes of strychnine were

injected through the anus into the rectum. After eight minutes a brisk tetanus carried the rabbit off. At the autopsy the entire stomach was taken out. The stomach was transparent, the level of the fluid was distinctly visible and changed easily with each change in the position of the stomach. On opening the stomach, the contents flowed out easily, no food clung to the mucous membrane, and where the coloured strychnine touched the mucous membrane there were distinct marks of the indigo carmine superficially adherent to the epithelial layer.

In this experiment the strychnine was surely in close contact with the mucous membrane of the stomach, and the vessels of the cardiac end were also not ligated; nevertheless no absorption took place.

Exp. 40.—Rabbit, 2,100 grammes, cardia tied; tube passed through duodenum into the pyloric part of the stomach; injected 50 milligrammes of strychnine, coloured with indigo carmine, directed to the front wall of the pyloric part; this part bulged up, tube removed, and pylorus tied. After two hours and five minutes, still no effect. Now 5 milligrammes of strychnine, coloured with methylene blue, was injected into the front wall of the stomach between the muscularis and the mucosa; a blue-stained area appeared, but no drop of the fluid escaped. After two minutes, a stormy tetanus broke in like lightning, and the rabbit was dead.

This shows strikingly that the ligation of the cardiac and the pyloric ends of the stomach does not prevent in the slightest the lymphatics and the blood vessels from carrying into the circulation the fluid which reaches them.

In sharp contrast to our results with strychnine, we found that the stomach of the rabbit promptly absorbs prussic acid.

Exp. 6.—Large rabbit, not starved, cardia tied; tube introduced through the duodenum into the stomach; injected 100 milligrammes of hydrocyanic acid (5 cubic centimetres of the official two-per-cent solution), coloured with indigo carmine; tube removed and pylorus tied. Rabbit soon shows uneasiness, the breathing becomes laboured, clonic convulsions set in, and the animal dies in fifteen minutes.

Exp. 26.—Rabbit, 2,200 grammes, not starved, cardia ligated; tube passed through duodenum; injected into the fundus 60 milligrammes of

prussic acid; tube removed and pylorus tied. Rabbit dies after twelve minutes in the same manner as in the former experiment.

At the autopsies of some of the rabbits which died from prussic acid, distinct hæmorrhagic surfaces were found on the mucous membrane of the stomach. This probably accounts for the good absorption of the prussic acid. The fact that hydrocyanic acid was constantly absorbed from the ligated stomach of the unstarved rabbits shows that the acid easily reaches the mucous membrane even in a full stomach, and, further, that the ligation alone does not prevent the blood vessels and the lymphatics from absorbing fluids which come within their reach. I have, therefore, in a few experiments with strychnine used the absorption of hydrocyanic acid as a test for the points in question.

Exp. 12.—Very large rabbit, 3,200 grammes, starved twenty-four hours, cardia tied; introduced tube through duodenum into the stomach, and pylorus tied tightly around tube. At 5.12 P. M. injected 50 milligrammes of strychnine in 10 cubic centimetres of water; at 8.28 rabbit perfectly quiet; injected again 50 milligrammes in 10 cubic centimetres of alcohol (fifty per cent). At 9.28 rabbit sleeps well; no sign of strychnine effect. Injected now 100 milligrammes of prussic acid in an alcoholic solution; rabbit soon starts breathing irregularly; short inspirations; convulsive expirations, with long intermission; heart first slow, then very rapid, growing imperceptible; some clonic convulsions; no hyperæsthesia; no tetanic or tonic contractions; rabbit dies gradually within twenty minutes.

Exp. 42.—Rabbit, 1,740 grammes, cardia tied; tube through duodenum into stomach; injected 200 milligrammes of strychnine in 20 cubic centimetres of water; tube removed and pylorus tied. After an hour and fifty minutes no effects whatsoever; 60 milligrammes of prussic acid, coloured with methylene blue, were now injected by means of a hypodermic needle, thrust through the front wall of the stomach, directly into the mass of food; the fine opening clamped; nothing escaped. Very soon after the veins on the walls of the stomach present a bright brick-red colour; the same was seen on the edges of the spleen; irregular laboured breathing set in; some clonic convulsions appeared without the presence of any hyperæsthesia; the rabbit died within twelve minutes.

The death was certainly due to the prussic acid, which rapidly reached the mucous membrane, penetrated it, and was carried off by the lymphatics and the blood vessels into the circulation. The enormously large dose of strychnine has probably also reached the mucous membrane, and would also have been carried into the circulation if it could only penetrate the epithelial layer to reach the lymphatics and the blood vessels.

I append two more experiments to show the character of absorption in some other parts of the alimentary canal.

Exp. 23.—Large rabbit, cardia tied; tube passed through duodenum into the stomach; injected 40 milligrammes of strychnine in a thirty-three-per-cent alcoholic solution; tube removed and pylorus tied. After eight hours no effect. Then 14 milligrammes of strychnine were injected into the œsophagus, the upper end of which was tied. After an hour and thirty-five minutes, still no effect. Now 4 milligrammes of strychnine were injected into the pharynx; in four minutes a brisk tetanus broke in, which ended fatally. Of course, it can not be stated whether the absorption has taken place only within the pharynx or also in the mouth, and perhaps even only in the mouth alone, though the injection was made directly into the pharynx.

Exp. 19.—Middle-sized rabbit, œsophagus tied at the upper end and also below the diaphragm. The vagi and the inferior laryngeal nerves were avoided. Through a cannula tied in the œsophagus several injections were made. At first only 4 milligrammes of strychnine were injected; half an hour later 4 milligrammes more were added, and forty minutes after this again 10 milligrammes were injected. An hour and fifteen minutes passed after the last injection with no sign even of increased irritability. Now 4 milligrammes of strychnine were injected into a loop of the small intestine; after seven minutes there was already marked hyperæsthesia, and five minutes later a stormy tetanus caused death.

I have to add that in one experiment half an hour after injection of 10 milligrammes of strychnine into the œsophagus, a tetanic attack did take place, but the œsophagus in this case was very much distended by air, which surely facilitates the absorption.

The results of my experiments, briefly summed up, are as follows:

The introduction of 6 to 10 milligrammes of strychnine into the full stomach of a rabbit with pylorus open is sure to bring on a tetanus within a short time. The effect is probably brought about by the rapid passage of the strychnine from the stomach into the intestine, whence it becomes absorbed in a few minutes.

When the pylorus, however, is closed, even such large doses as 200 milligrammes of strychnine, remaining for many hours within an empty stomach, with good circulation and with intact innervation of the vagi, do not produce any effect at all. It seems that the mucous membrane of the stomach does not absorb even the smallest fraction of the strychnine. Next to the stomach, we also found that the mucous membrane of the œsophagus absorbs strychnine very poorly.

The pharynx is apparently the part of the alimentary canal which absorbs best; 3 to 4 milligrammes in the pharynx will induce a tetanus in three to four minutes.

The rectum absorbs nearly as well as the pharynx, as 3 milligrammes injected through the anus will call forth a tetanus in six to eight minutes. The absorption seems to take place here even better than in the small intestine, as it takes twelve to fifteen minutes before a tetanus breaks out after an injection of 4 to 5 milligrammes of strychnine into a loop of the small intestine.

Prussic acid is absorbed very well from the stomach even when the pylorus is ligated. It seems to produce a hæmorrhagic surface on the mucous membrane, which facilitates the absorption. Possibly, also, the volatility of prussic acid may favour prompt absorption, as gases seem to be readily absorbed in the stomach.

[*Studies from the Physiological Laboratory of Columbia University at the College of Physicians and Surgeons, New York City, vol. ii.*]

THE INFLUENCE OF PHLORIDZIN ON THE BILE AND LYMPH.

By PHOEBUS A. LEVENE, M. D.

(*From the Department of Physiology of Columbia University at the College of Physicians and Surgeons, New York.*)

In my article on Phloridzin Glycosuria, published in 1894,* I had in view the demonstration of two propositions: (1) That there existed no sufficient grounds for v. Noorden's assumption that phloridzin glycosuria does not at all resemble any forms of spontaneous diabetes mellitus, and that, therefore, the mechanism of this experimental glycosuria cannot be applied to the explanation of any clinical forms of diabetes; and (2) that the appearance of sugar in the urine in this experimental glycosuria could not be satisfactorily explained by mere elimination from the blood.

Several facts had led me to doubt the "elimination theory." In the first place v. Mering himself, who examined the blood for sugar only after the injection of phloridzin, found that the amount of sugar did not differ much from that which occurs very often in normal dogs, and therefore could not be called subnormal. Again, the work of Minkowski proved that after the extirpation of the kidneys and subsequent phloridzin injection there was in fact some slight increase of sugar in the blood. Lastly, Cornevin found an increase of sugar in the milk after phloridzin injection. To these facts I was able to add from my own experiments that the venous blood of the kidneys never contained less sugar than the arterial, and that the amount of sugar in the whole kidney after the phloridzin injection was higher than normal.

Very recently Zuntz, again recurring to the study of "phloridzin diabetes," has shown in a very ingenious way that the appearance of

* References to the literature are at the end of this article.

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sugar in the urine after phloridzin injection may be due exclusively to the activity of the kidneys. This investigator injected very small quantities of phloridzin directly into the renal artery and afterward collected the urine of each ureter separately. He found that the urine of the kidney into which phloridzin had been injected contained sugar almost immediately, whereas in the other it was demonstrable only after some time, and then in much smaller quantities. Zuntz attempted further to limit the action of phloridzin to one kidney only, and therefore ligated the renal veins of the side upon which the glucoside was injected. But immediately after ligation the secretion of urine of the corresponding kidney was suppressed and sugar at once appeared in the urine of the other kidney, where without ligation it was usually demonstrable only after some time.

In these later experiments Zuntz sees a new corroboration of the elimination theory of v. Mering and a new disproof of the supposition expressed in my previous article.

Zuntz says:

"Verfasser hat die Nierenvene behufs Einführung einer Canüle abgeklemmt. Darnach aber hört die Urinsecretion für längere Zeit auf, es kann also auch keine Abnahme des Zuckergehaltes in der Vene erwartet werden. Noch weniger berechtigt ist Levene aus dem erhöhten Zuckergehalt der Niere selbst auf eine Beziehung derselben zur Zuckerbildung zu schliessen. Unvermeidlich findet sich in dem Canalsystem der Niere eine gewisse Menge Urin; da dieser Urin nach Phloridzinzufuhr 10 pro cent und mehr Zucker enthält, muss die Zuckerbestimmung in der gesammten Niere einen höheren Gehalt ergeben, als bei normalen Thieren, ohne dass man daraus folgern darf, der Zucker sei im Nierenparenchym gebildet worden."

But, if the suppression of the secretion of the urine immediately after stagnation actually takes place, this fact by itself does not by any means show that all the functions of the renal epithelium are suppressed at the same time, and there is no reason why the epithelium, stimulated or influenced in some way by the glucoside, could not for a time at any rate continue to absorb sugar from the blood.

Beyond doubt Zuntz's experiment affords a very striking argument

in favor of the supposition that the appearance of sugar in the urine after administration of phloridzin can be produced by the kidneys alone. Nevertheless by itself it proves nothing more, and fails utterly to explain the way in which the kidneys produce this effect. The latter might just as well be due to mere elimination as to local overproduction of sugar in the kidney. Important, therefore, as is Zuntz's discovery in showing the possibility of the occurrence of renal diabetes, it does not add much to the previous facts at our command for the explanation of the mechanism of phloridzin glycosuria.

The fact discovered by Zuntz, that the time which elapses between the injection of phloridzin directly into the arteries of the kidneys and the appearance of sugar in the urine is so short, induced me to attempt to apply the same method to another secretory organ, in order to see whether or not it would respond to the stimulus in the same way as the kidneys. As I have stated before, there is some mention in the literature that the mammary glands resemble the kidneys in this respect.

I chose for this purpose the liver. The experiments were conducted in the following way: The animals were narcotized by means of ether. After the gall bladder had been emptied of its contents a cannula was inserted into it and a few cubic centimetres of a 0.5 per cent solution of phloridzin in alkaline water were injected directly into the portal vein. The specimens of bile collected before and at different times after the injection were separately treated with 10 volumes of 95 per cent alcohol for 24 hours and filtered. The filtrate was decolorized by means of bone-black, evaporated to dryness, dissolved in water, filtered, and the resulting filtrate was tested with Fehling's solution. The experiment was repeated on five dogs. In two of them the blood-vessels of the kidneys were ligated previous to the injection of phloridzin. In all cases a very distinct reduction of the copper appeared with bile collected after the injection. In some cases a slight reduction took place also in the normal bile; this was probably due to the effects of the anæsthetic, and was never so great as in the other cases. As the amount of sugar in the bile was not quite sufficient for a quantitative examination, I decided to observe the influence of

phloridzin injection on animals with biliary fistulæ, where I could collect pure bile without inconvenience to the animal and hence without the use of narcotics. I performed this operation on two dogs with the following results:

Experiment, February 17, 1896.—Dog: weight, 20 kilos; operation for biliary fistula performed under anæsthesia. The cannula was kept open till the following morning, when it was closed. February 18, 11 A. M.: the normal bile was collected and a solution of 2.5 grammes of phloridzin in alkaline water was injected hypodermically. At 3 P. M. 25 cubic centimetres of bile were collected. At 6 P. M. 19 cubic centimetres of bile were collected. The cannula was left open till the following morning, when it was again closed for a few hours and the bile collected. These operations were repeated until February 21, when the dog was killed, as a slight suppuration had taken place around the wound. All the specimens of bile were treated in the above-mentioned way. Reduction of the copper solution took place in all after the injection of phloridzin, but did not appear in the normal bile. On February 21 the urine still possessed high reducing power.

Experiment, March 24, 1896.—Dog: weight, 9 kilos; operation for biliary fistula performed under anæsthesia: the fistula was left open until the following morning. March 25, 10 cubic centimetres of normal bile were obtained and a solution containing 2 grammes of phloridzin was given to the dog by the mouth: a portion was vomited. At 3 P. M. 7 cubic centimetres of bile were collected. As the quantity of bile secreted thereafter was very small, the dog was killed. The bile obtained before the injection of phloridzin possessed no reducing power, that after the injection showed a distinct reduction.

Though it is worthy of note that the reducing power of the bile was never so high as that of the urine, it must be remembered that the question for me was whether phloridzin acts exclusively on the kidneys or not. The foregoing experiments, as well as those of Cornevin, tend to answer the question in the negative. On the other hand these facts alone do not exclude the elimination theory.

In order to obtain more data relating to the cause of the appearance of sugar in the urine and other secretions, I decided to examine the lymph of the thoracic duct. I thought that over-production of sugar might coexist with a normal percentage of sugar in the blood

by virtue of the glycolytic power of the blood, which in this case might be increased. In such case one would expect to find the amount of sugar in the lymph increased after the injection of phloridzin. The experiment was conducted in the following way: The animals were allowed to fast for at least 24 hours previous to the operation. They were narcotized by means of morphine and ether. In all the operations artificial respiration was employed. In order to prevent coagulation the lymph was collected in a saturated solution of Na_2SO_4, which was then boiled with a few drops of acetic acid. The precipitate was once more boiled with a saturated solution of Na_2SO_4, again filtered, and the precipitate again washed with a hot Na_2SO_4 solution. All the filtrates and wash waters were combined, and the sugars determined by means of the following modification of Ahlin's method, which I have used for the last two years.

As in Ahlin's method, an excess of Fehling's solution was taken. After the reduction of the copper, the excess of the Fehling's solution was decanted on an asbestos filter, and the main part of the residue was left in the evaporating dish. The residue was then washed and the wash water decanted again. The precipitate of Cu_2O on the asbestos filter was also washed; and the Cu_2O in the dish and that on the filter were dissolved by means of nitric acid, and mixed together. After it had been neutralized by means of sodium carbonate, a few drops of ammonia were added to the solution, which was then titrated by means of a standard solution of KCy. This method has also been in use for the last year in the Analytical Laboratory of the School of Mines of the Columbia University of New York. The results of these experiments may be summarized as follows:

Experiment 1, *April* 17.—Dog; weight, 7 kilos; no food for 48 hours previous to the operation; 0.05 gramme of morphine two hours before the operation; ether; artificial respiration. A cannula was inserted into the thoracic duct. During the first thirty minutes 24.1 grammes of lymph were collected. Then 20 cubic centimetres of a 2 per cent solution of phloridzin in alkaline water were gradually injected into the right jugular vein, and in the next twenty minutes 36.2 grammes of lymph were collected. The urine obtained from the ureter contained sugar.

The amount of Cu reduced by the lymph before injection of phloridzin = 0.0313 gramme, corresponding to 0.078 per cent of sugar.

The amount of Cu reduced by the lymph after injection of phloridzin = 0.0686 gramme, corresponding to 0.0967 per cent of sugar.

In this case the first lymph was not collected in Na_2SO_4 at once, but was only later transferred to this solution, the greater part being then coagulated.

Experiment 2, *May* 27.—Dog; weight, 20 kilos; fasting about 24 hours previous to the operation; 0.15 gramme of morphine administered about two hours before the operation. During the first thirty-five minutes 24 grammes of lymph were collected; 28 cubic centimetres of a 2 per cent solution of phloridzin in alkaline water were then gradually injected into the right jugular vein. The lymph collected in the next twenty minutes was lost, but a third portion was collected during forty minutes equal to 43.6 grammes.

The amount of Cu reduced by the first lymph = 0.098 gramme = 0.279 per cent of glucose.

The amount of Cu reduced by the second lymph = 0.0634 gramme = 0.074 per cent of glucose.

Experiment 3, *June* 1.—Dog; weight, 10 kilos; fasting 48 hours previous to the operation; 0.1 gramme morphine injected two hours before the operation. During the first thirty minutes after the operation 10 grammes of lymph were collected. 30 cubic centimetres of a 1 per cent solution of phloridzin were then injected into the right jugular vein. In the next forty-five minutes 22.5 grammes of lymph were collected.

The amount of Cu reduced by the first lymph = 0.049 gramme = 0.259 per cent of glucose.

The amount of Cu reduced by the second lymph = 0.078 gramme = 0.177 per cent of glucose.

Experiment 4, *June* 2.—Dog; weight, 18 kilos; fasting 24 hours previous to the operation; 0.15 gramme of morphine injected one hour before the operation. During the first twenty-five minutes after the operation 29.3 grammes of lymph were collected. 0.4 gramme of phloridzin in 20 cubic centimetres of very dilute Na_2CO_3 solution was injected into the jugular vein. In the next 15 minutes 27.4 grammes of lymph were collected.

The amount of Cu reduced by the first lymph = 0.0625 gramme = 0.110 per cent of glucose. (Part of the Cu solution prepared for titration was lost during neutralization.)

The amount of Cu reduced by the second lymph = 0.0666 gramme = 0.125 per cent of glucose.

Experiment 5, June 4.—Dog; weight, 12 kilos; fasting 24 hours before the operation; 0.15 gramme of morphine injected two hours before the operation. During the first twenty minutes after the operation 24.6 grammes of lymph were collected. 0.4 gramme of phloridzin in 30 cubic centimetres of H_2O containing some Na_2CO_3 was injected into the right jugular vein.

The amount of Cu reduced by the first lymph = 0.095 gramme = 0.196 per cent of glucose.

The amount of Cu reduced by the second lymph = 0.078 gramme = 0.175 per cent of glucose.

Experiment 6, June 8.—Dog; weight, 20 kilos; fasting twenty-four hours before the operation; 0.15 gramme of morphine injected two hours before the operation. During the first thirty-five minutes 3 grammes of lymph were collected. 0.3 gramme of phloridzin dissolved in 30 cubic centimetres of H_2O containing some Na_2CO_3 was then injected. During the next 45 minutes 10 grammes of lymph were collected.

The amount of Cu reduced by the first lymph = 0.0161 gramme = 0.300 per cent of glucose.

The amount of Cu reduced by the second lymph = 0.0397 gramme = 0.130 per cent of glucose.

The results are here grouped in tabular form.

No.	Percentage of Glucose in the lymph before injection of phloridzin.	Percentage of Glucose in the lymph after injection of phloridzin.	Difference expressed in percentages.
1	0.078	0.096	+ 23
2	0.279	0.074	- 73
3	0.259	0.177	— 32
4	(0.110) part lost	0.125	— ?
5	0.196	0.175	— 11
6	0.300	0.130	— 57

All these experiments except No. 1 indicate a considerable decrease of sugar in the lymph after the injection of phloridzin.

In order to ascertain the relation of this decrease of glucose in the lymph to the activity of the kidneys, I thought it advisable to ligate the whole hylus renalis previous to the collection of the lymph and the injection of the phloridzin; and, in order to determine to what extent this decrease might be due to the action of phloridzin, I examined the lymph collected in the same intervals as in the other experiments, but without the injection of the glucoside. Unfortu-

nately I did not have time to perform each of these control operations more than once.

Experiment, June 12, 1896.—Dog; weight, 18 kilos; fasting twenty-four hours before the operation; 0.1 gramme morphine injected two hours before the operation. The dog was narcotized, artificial respiration was employed; both hyli renales were ligated. The operation was then directed to the thoracic duct. During the first 30 minutes 13 grammes of lymph were collected. 0.5 gramme of phloridzin in 40 cubic centimetres of H_2O containing some Na_2CO_3 was injected into the jugular vein, and in the next thirty minutes 19.5 grammes of lymph were collected.

The amount of Cu reduced by the first lymph = 0.063 gramme = 0.240 per cent of glucose.

The amount of Cu reduced by the second lymph = 0.568 gramme = 0.150 per cent of glucose.

Control Experiment, June 18, 1896.—Dog; weight, 18 kilos; no phloridzin injected. The operation was performed in the usual way with anæsthetics and artificial respiration. During the first 35 minutes 16.5 grammes of lymph were collected, during the following 35 minutes 15 grammes.

The amount of Cu reduced by the first lymph = 0.0725 gramme = 0.224 per cent of glucose.

The amount of Cu reduced by the second lymph = 0.0706 gramme = 0.240 per cent of glucose.

The foregoing experiments tend to show that the kidneys are not the only organs affected by phloridzin. This conclusion is based not only upon the result of phloridzin injection on the bile and the milk, but also upon the fact that the amount of sugar in the lymph decreases after the injection of phloridzin, even if the hyli renales are ligated previous to the injection of the glucoside.

The examination of the lymph shows a decrease of sugar after the administration of the phloridzin. If this is to be explained by the fact that the blood, being more than normally deprived of sugar by one organ, yields less to the other tissues, and, therefore, the lymph flowing from those tissues is poorer in sugar than under normal conditions, we have a strong argument in support of the elimination theory. But, on the other hand, it has been found that the urine

can eliminate during one hour after the administration of phloridzin more sugar than can be obtained from the daily amount of lymph. This fact, especially when taken in conjunction with the changes taking place in the different tissues and in the metabolism of the whole organism, offers at present some room for doubt in regard to the elimination theory. The same opinion has been expressed by Kraus.* At the same time the occurrence of spontaneous diabetes without hyperglycæmia, which has been proved by Seegen, does not justify v. Noorden in his assertion that the mechanism of phloridzin glycosuria does not resemble any form of spontaneous diabetes. Only recently Klemperer, at the meeting of the Verein für innere Medicin in Berlin (May 18, 1896), has called attention to a form of renal diabetes resembling the phloridzin glycosuria.

As to Zuntz's supposition of the existence of a certain mechanism regulating the amount of sugar in the blood through increased or decreased combustion of the sugar, I may remark that the study of phloridzin glycosuria has made virtually the same impression on myself, and I expressed in my previous paper the following opinion: "The absence of hyperglycaemia may be explained by the supposition that the organism has not lost its ability to rid itself of the superabundance of sugar on the one hand by its elimination through the kidneys, and on the other by its increased decomposition."

I wish to express my thanks to Professors J. G. Curtis and F. S. Lee for their kindness to me during my work in their laboratory.

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STUDIES FROM THE DEPARTMENT OF PHYSIOLOGY OF COLUMBIA UNIVERSITY AT THE COLLEGE OF PHYSICIANS AND SURGEONS, NEW YORK, VOL. I.

THE BACTERICIDAL ACTION OF LYMPH TAKEN FROM THE THORACIC DUCT OF THE DOG.

By S. J. MELTZER, M. D., and CHARLES NORRIS, M. D.
(*From the Physiological and Pathological Departments of the College of Physicians and Surgeons, Columbia University, New York.*)

Nine years ago Nuttall* first described the bactericidal action of the blood, suggesting at the same time that the other fluids of the body may possess a similar action. He found later that the aqueous humor, pericardial fluid, and a pleuritic fluid poor in cellular elements also possessed bactericidal power. Prudden† determined that ascitic fluid, fluid taken from a hydrocele, and the liquor amnii of the pig had the same properties.

As far as we have been able to ascertain, no systematic examination of all the body fluids, in regard to this point, has ever been made.

Flexner‡ found that the blood serum of the human placenta was not distinctly germicidal for the Staphylococcus aureus, but was germicidal for the Bacillus typhosus. Caution in drawing conclusions as to the germicidal action of body fluids not hitherto examined is manifestly necessary. A controversy having lately arisen as to the channels of absorption of serous fluids, it seemed to us a matter of importance to determine whether lymph from the thoracic duct possesses bactericidal powers. The possibility was present that an exchange of the bactericidal factors between the blood and lymph—lymph from the interstitial spaces—might occur only through the walls of the blood-vessels. Lymph from the thoracic duct might not therefore possess any action. At the beginning of our work, Professor Prudden called our attention to an article by Max Neisser,§ entitled

* Nuttall, *Zeitschr. f. Hygiene*, iv, 353.

† Prudden, On the Germicidal Action of Blood Serum and other Body Fluids. *Medical Record*, Jan. 25, 1890.

‡ Flexner, *Journal of Experimental Medicine*, i, 576.

§ Neisser, *Zeitschr. f. Hygiene*, xxii, 12.

"Ueber die Durchgängigkeit der Darmwand für Bakterien." In this article Neisser devotes barely ten lines to this question, but nevertheless comes to the conclusion that lymph from the thoracic duct of the dog possesses no germicidal action.

From a scientific point of view it seems important to determine accurately whether lymph, as well as blood, is germicidal, especially as the conclusions of Neisser upon this subject are open to criticism.

The bacteria studied by Neisser with reference to this point were Bacillus prodigiosus, Staphylococcus pyogenes aureus, Bacillus pyocyaneus, and a bacillus resembling Bacillus typhosus. Nissen* furnishes a statement showing the bactericidal power of the blood on Bacillus prodigiosus. Original plate 3000 to 4000, after three hours 2800, after five hours 10,200, after twenty hours innumerable. According to this result blood can hardly be considered to have much germicidal action on this bacillus. In regard to the Staphylococcus aureus, most authors have found that its growth is but little impaired by normal blood, but Flexner† has demonstrated that normal human blood serum may exert decided germicidal action upon this organism. Buchner‡ mentions that the Bacillus pyocyaneus and a bacillus of the typhoid group cultivated from the feces are among the most resistant of the bacteria which he studied, to the action of blood serum. There is no evidence that Neisser's bacillus was identical with that of Buchner, but it certainly would have been well to determine previously the effect of blood serum upon the former. Neisser thus employed organisms over which the blood itself seems to have little or no germicidal power. In testing the germicidal action of lymph and other body fluids, the germicidal action of the blood must be taken as a standard for comparison. When fluids are found to possess no germicidal power over organisms which are likewise resistant to blood, the conclusion is not justifiable that the former fluids possess no bactericidal action. Furthermore, Neisser thus describes his primitive methods of research:§ "Sie wurden theils direct in den Chylus verimpft, theils wurde der Nährboden mit Chylus reichlich vermengt, theils wurden steril gebliebene Versuchsplatten nachträglich mit den Bakterien bestrichen, auf keine Weise aber war eine Behinderung des Bakterienwachsthums nachweisbar." With this imperfect method of experimentation the germicidal action of blood would hardly have been discovered.

* Nissen, *Zeitschr. f. Hygiene*, vi, 488.
† Flexner, op. cit., p. 574.
‡ Buchner, *Centralbl. f. Bakteriol.*, v, 821.
§ Neisser, op. cit., p. 20.

In our investigations the typhoid bacillus was alone tested. This bacillus had been tested by most of the observers working on the germicidal power of the blood, and our main purpose was to establish the presence or absence of any such power in the lymph. The methods employed by us were those followed by Nuttall and others and the method used by Buchner.

It was essential to obtain fluid lymph, as only in this condition can it be readily handled and measured. A sterilized glass cannula bent at right angles is firmly tied in the thoracic duct. The free end of the cannula is then inserted in the neck of a bottle containing glass beads, bottle and beads both having been previously sterilized. After collecting the lymph the bottle is closed with a sterilized glass stopper and vigorously shaken for several minutes. The lymph remains fluid, is poured into test tubes and kept ready for use in an ice chest.

We will not speak of our attempts to obtain fluid lymph by injecting peptone into the circulation or by collecting the lymph in solutions of sodium sulphate or sodium oxalate.

Tying the cannula in the duct and obtaining sterile lymph constitute by no means an easy task, and several of our attempts were unsuccessful. In all our experiments here reported the lymph was proved beyond doubt to be sterile by inoculations in nutrient gelatin and agar watched for three days. We were occasionally obliged to keep the lymph a day or two before testing it. Positive results, however, gain in importance through this circumstance. All the dogs fasted from 30 to 36 hours before being operated upon. The chyle from dogs recently fed is not suitable, as the fine fat droplets interfere in counting colonies on the plates. Artificial respiration was used to stimulate the flow of lymph. In two of the dogs normal salt solution was injected intravenously, whereby a thinner lymph was obtained. In several, small doses of curare were injected. Before and after the flowing of the lymph, specimens of blood were also collected. Unfortunately we were not always able to make parallel tests.

The following results were obtained by the method developed and first employed by Nuttall. 1 cc. of the lymph is pipetted off into a

number of test tubes. 5 cc. of sterilized normal salt solution are inoculated with several loops of a typhoid bouillon culture, thoroughly shaken to insure equal distribution of bacilli throughout the fluid. A fluid gelatin tube under 40° C. is then inoculated with two or three loops of the suspension in salt solution. The gelatin is mixed and poured, this plate serving as the control. All the lymph tubes are then inoculated with the same number of loops of the salt solution and are placed in the thermostat. At the end of the allotted time each lymph tube on removal from the thermostat receives 5 cc. of fluid gelatin (under 40° C.), is then well shaken and poured into a Petri dish. All the plates are kept on a dark shelf at room temperature and the colonies are counted after three days' growth. This method is designated as Nuttall's.

EXPERIMENT F. *Nuttall.*

	Control.	1 hr.	5 hrs.	22 hrs.
Lymph	184	382	20	0

EXPERIMENT G. *Nuttall.*

	Control.	1 hr.	17 hrs.	24 hrs.
Lymph	96	67	18	5

EXPERIMENT K. *Nuttall.*

	Control.	1¼ hrs.	4 hrs.	25 hrs.	48 hrs.	72 hrs.
Lymph	127	15	0	0	0	0

In these experiments the germicidal action of the lymph is apparent. The question presented itself, however, whether the disappearance of the bacilli could not be explained by the lack of suitable nutrient material in the lymph. It might be suggested that the lymph does not kill the bacilli, but that the latter only die from want of suitable nourishment. Although this supposition is extremely improbable, we used two further media for control, one consisting of a normal salt solution containing 1 per cent of bouillon, designated as salt bouillon, of which 0.5 cc. was always used; the other known as lymph bouillon, consisting of 1 cc. of the above salt bouillon, plus 0.5 cc. of lymph.

EXPERIMENT L. *Nuttall.*

	Control.	2 hrs.	5 hrs.	25 hrs.	48 hrs.
Lymph	4130	3339	815	5130	7727
Lymph bouillon	4130	1938	1250	8650	∞
Salt bouillon	4130	5406	25440	∞	∞

EXPERIMENT M. *Nuttall.*

	Control.	2½ hrs.	5½ hrs.	24 hrs.
Lymph	1043	334	264	0
Lymph bouillon	1043	318	215	0
Salt bouillon	1043	11720	9349*	∞
Blood (after flow of lymph)	1043	114	5	140

* Hard to count, colonies spreading on soft gelatin, probably more numerous.

In both experiments growth in the salt bouillon is immediate, the plates soon becoming overcrowded, whereas in the lymph bouillon plates a steady decrease is observed. In Experiment M the 24-hour lymph bouillon and lymph plates are sterile; both series of plates are strikingly similar. In Experiment L, after 25 hours in the thermostat the bacilli begin to grow. This observation corresponds with those already made with the blood, namely, that when the germicidal factors have not been powerful enough to kill all the bacteria, the more resistant surviving forms later begin to grow, and the faster the better the nutritive media presented them. In Experiment L the growth takes place more rapidly in the lymph bouillon than in the plain lymph. The effect of the original number of bacilli on the final result should also be noted. The smaller the number of bacilli exposed to the action of the lymph the sooner are sterile plates obtained. In Experiment L, where the original showed 4130 colonies, a marked decrease alone was observed, the more resistant forms rapidly growing again.

Our next results were obtained mainly by Buchner's method. In each of three sterile test tubes 4 cc. of lymph were introduced. In order to study the effect of heat on the germicidal power of lymph we subjected one of the tubes to half an hour's heat at 56° C. All tubes were inoculated with a typhoid bouillon culture; after shaking, controls were at once made by inoculating melted gelatin tubes with three loops of the lymph. After controls from each of the lymph tubes were made, one tube was kept at room temperature, and the lymph

tube which had been heated for half an hour and the third tube were both placed in the thermostat at 37° C. From all three tubes at regular intervals gelatin tubes were inoculated with the same loop and plates poured. This method is designated as Buchner's. In most of the experiments Nuttall's method was also pursued.

EXPERIMENT N. *Buchner.*

	Control.	1 hr.	3 hrs.	5½ hrs.	24 hrs.	53 hrs.
Lymph 37°	1272	1462	445	3975	45792	∝
Lymph 22°	1481	1580	1106	636	7822	∝
Lymph (heated at 56°) 37°	973	1634	2569	7741	42930	∝
Blood serum,* ante, 37°	1284	775	362	1199	∝	
Blood serum,† post, 37°	2143	2032	1641	∝	∝	

*4 cc. †2 cc.

EXPERIMENT N. *Nuttall.*

	Control.	1 hr.	7 hrs.	27 hrs.	48 hrs.
Lymph* 37° C.	886	780	216	0	9471

*Seven days in ice chest before testing.

EXPERIMENT P. *Buchner.*

	Control.	1 hr.	4½ hrs.	26 hrs.
Lymph 37°	1319	550	70	78
Lymph 22°	1648	1399	455	225
Lymph (heated at 56°) 37°	2117	2308	4704	∝
Blood serum, ante, 37°	5083	2026	270	∝
Blood serum, post, 37°	2181	1461	270	∝

EXPERIMENT P. *Nuttall.*

	Control.	1 hr.	2 hrs.	5 hrs.	24 hrs.
Lymph	∝	40068	36061	5787	34344
Lymph bouillon	∝	51643	55014	27475	∝
Blood serum, ante	∝	32626	20606	18899	∝
Blood serum, post	∝	28620	21751	8295	∝

EXPERIMENT R. *Buchner.*

	Control.	1 hr.	4 hrs.	19 hrs.	24 hrs.	72 hrs.
Lymph 37°	906	340	101	196	710	∝
Lymph 22°	1484	969	466	122	89	190
Lymph (56°) 37°	975	954	1643	∝	∝	∝
Blood serum 37°	1696	1229	325	∝	∝	∝
Blood serum 22°	1240	1246	1023	405	217	∝

EXPERIMENT R. *Nuttall.*

	Control.	1 hr.	3 hrs.	5 hrs.	24 hrs.	72 hrs.
Lymph	1310	296	177	140	110	∝
Lymph bouillon	1310	334	140	66	110	6360
Salt bouillon	1310	1900	1060	7268	∝	∝

In Experiment R the lymph was obtained half an hour after the death of the dog. The lymph flowed fifty minutes with the aid of artificial respiration. The blood was obtained out of the central end of the jugular vein.

EXPERIMENT O. *Buchner.*

	Control.	1 hr.	3 hrs.	6 hrs.	26 hrs.
Lymph 37°	1368	1163	3048	16854	∞
Lymph 22°	998	1188	786	1812	∞
Lymph (56°) 37°	1717	1807	2862	∞	∞

EXPERIMENT O. *Nuttall.*

	Control.	1 hr.	3 hrs.	6 hrs.	25 hrs.
Lymph	2353	4293	∞	∞	∞
Lymph bouillon	2353	7504	∞	∞	∞
Salt bouillon	2353	2925	4897	5533	1106

EXPERIMENT O. *Buchner.*

	Control.	1 hr.	3 hrs.	26 hrs.
Blood serum 37°	909	1507	1596	∞
Blood serum 22°	1125	858	975	∞

In Experiment O the blood and lymph remained nineteen days in the ice chest before being tested.

Our results, we believe, justify the conclusion that lymph from the thoracic duct of the dog possesses marked germicidal action on the typhoid bacillus. A noticeable decrease in the number of colonies in the lymph plates is observed, the decrease being the more marked the longer the exposure to the action of the lymph.

The decrease cannot be accounted for simply on account of lack of suitable nutrient material in the lymph, and for the following reasons: The lymph bouillon plates show the same immediate decrease in the number of colonies as do the pure lymph plates, whereas the bouillon salt solution at once shows a marked increase in growth. The addition of lymph produces a direct inhibitory action on the growth of the typhoid bacillus. The germicidal action of lymph is destroyed by too long standing (nineteen days in Experiment O) and by heating for half an hour at 56° C. The lymph after such treatment furnishes a good medium. The action of the lymph is most apparent when the number of bacilli inoculated in the lymph is relatively small. (Compare Experiments F and P: in Experiment F, starting with 184, after twenty-two hours the plate is sterile; in Experiment P (Nuttall) with an

overcrowded original plate a temporary relative diminution alone is observed, growth soon beginning anew.) The quantity of the lymph must also be considered. The greater the quantity of lymph with the same inoculation the more apparent does the action of the lymph become. The bactericidal power of the lymph was rendered much more apparent by Nuttall's method than when Buchner's method was employed. In Buchner's method only two or three loops of lymph are transferred to the gelatin, and this small quantity can hardly continue to exercise any further action, whereas by Nuttall's method the dilution is only one-fifth or one-tenth of gelatin and the action of the lymph in such dilution may very well continue to retard the growth in the Petri dish.

The lymph possesses not merely an inhibitory action on the growth of the typhoid bacillus, but is definitely germicidal. We convinced ourselves of this fact by placing several of the sterile lymph plates in the thermostat. No growth was observed on any of the plates. On the other hand, we have seen lymph plates, which after 3 days' growth at room temperature were sterile, several days later develop a few small colonies, the control plates usually obtaining their full growth in 48 hours. The 5-hour plate in Experiment F furnishes an example. After 53 hours' growth it was sterile, 3 days later 20 colonies appeared. On the whole, a retardation in the appearance of the colonies on the lymph plates as compared with the control plate was always noticeable. The more resistant forms of the bacilli, *i. e.* those not destroyed by the lymph, were nevertheless inhibited in their growth. We believe, however, that the difference between partial and complete inhibition of growth is only a quantitative and not an essential one.

We do not feel justified in forming a positive opinion as to the comparative bactericidal powers of blood serum and lymph, as the number of our successful parallel experiments with lymph and blood serum has not been sufficiently numerous. The experiments here cited, as well as others not published because the lymph or blood serum was not obtained sterile, justify us in believing that the germicidal power of lymph is not much less than that of blood serum.

In one respect a difference between lymph and blood serum was

present in our experiments. The bactericidal action of blood serum diminished and disappeared sooner than did that of lymph. Perhaps blood serum furnishes a better medium for growth, and when the bactericidal property is exhausted the nutritive factors are enabled to gain the upper hand and thus determine a more rapid growth than with lymph.

During the course of our experiments the effect of room temperatures on the bactericidal action of lymph and blood serum was also noticed. Nuttall says "the temperature at which blood specimens after inoculation are kept appears, at least with rabbit's blood, between the limits of 19° and 38° C. to have little effect on the germicidal action." We have, however, obtained a different result. This is evident in a comparison of the development of the germicidal action of lymph and blood in Experiment R, where blood serum or lymph kept at room temperature developed its germicidal power more slowly but retained it longer than blood or lymph kept at 37° C.

STUDIES FROM THE DEPARTMENT OF PHYSIOLOGY OF COLUMBIA UNIVERSITY AT THE COLLEGE OF PHYSICIANS AND SURGEONS, NEW YORK, VOL. I.

NOTES ON THE PHYSIOLOGY OF THE CARDIAC NERVES OF THE OPOSSUM (DIDELPHYS VIRGINIANA).

By REID HUNT and D. W. HARRINGTON.

(From the Physiological Laboratory of Columbia University at the College of Physicians and Surgeons, New York.)

The knowledge of the physiology of the cardiac nerves has been derived from the study of such a very limited number of species that it is desirable to extend the study to other forms. So far as we are aware, no one has investigated the innervation of the heart of a marsupial; hence the following observations upon the opossum may be not without interest.

1. METHODS OF EXPERIMENTING.

As the opossum does not seem to have been used hitherto for physiological experiments, we shall record our observations in some detail.

It may be said that, in general, the opossum is a very favorable subject for physiological experiments; it is of convenient size, the blood-vessels are comparatively large and tough, the blood pressure is moderately high, and anæsthetics are remarkably well borne. In some of these respects the opossum offers marked advantages over the rabbit; on the other hand the large amount of fat which, as is well known, this animal tends to accumulate often makes operations very difficult.

In our experiments the blood pressure and the heart rate were recorded by the mercury manometer in the usual manner.

Anaesthetics.—We have used the following anæsthetics: ether, chloral hydrate (in doses of 1 grm.), morphia sulphate (in doses of .03-.04 grm.) and morphia sulphate and chloral hydrate combined in the proportion of .75 grm. of the latter to .01 grm. of the

Reprinted from the Journal of Experimental Medicine, Vol. II, No. 6.

former. The morphia and chloral were injected hypodermically. The above mentioned combination of morphia and chloral is probably the best anæsthetic for experiments upon the circulation; animals anæsthetized by it have a good blood pressure; the heart beat is strong and regular, and the vagi are in a condition of moderate tonicity, which seems to be their normal condition.

Normal blood pressure.—The blood pressure was determined only in animals anæsthetized by some of the above drugs; in such animals the arterial pressure, as determined by a cannula in one of the carotid arteries, varied from about 120 to 135 mm. of mercury. Curare affected the blood pressure but little.

Rate of the heart-beat.—The heart rate as determined in anæsthetized animals varied from 144 to 218 beats per minute, being lowest in animals under the influence of morphia alone and highest in etherized animals. When chloral was used, either alone or in combination with morphia, the rate of the beat was between the above mentioned figures. Determinations of the heart rate of the normal animal by means of the stethoscope were not very satisfactory; apparently, however, it was somewhat less than the above—about 120 per minute. Hence the anæsthetic or the operation necessary for the insertion of the cannula had increased the rate of the heart, most probably by diminishing the tonic activity of the vagi.

2. THE VAGUS.

Section of the vagi.—Section of the vagi was followed by results varying in the different experiments according to the degree to which the vagus centres were in activity, and this again varied with the anæsthetic employed. In animals under the influence of chloral or morphia an increase in the heart rate and a rise of blood pressure usually followed section of these nerves; in etherized animals there was little or no effect. Occasionally there was a rise of blood pressure although the heart rate was not affected. Such a rise of blood pressure without any change in the heart rate is not an infrequent occurrence in other animals; the most probable explanation of such cases is that there are fibres in the vagus which on being stimulated

are able to weaken the heart-beat, and that at times they are in a state of tonic activity or have been stimulated in some manner.*

Stimulation of the vagus.—The effects upon the heart of stimulating the peripheral end of the vagus of the opossum are essentially similar to those observed in other mammals; they differ markedly, however, in certain respects.

It seems to us that stimulation of the opossum's vagus is, as a rule, more efficient than is the case with the mammals ordinarily used in the laboratory. For instance, we have never failed to obtain a standstill of the heart by stimulating the vagus with induced currents of moderate intensity (secondary coil of an ordinary Du Bois-Reymond coil 9 to 12 cm. from the primary). As is well known, failure to obtain this result is frequently met with in cats† and occasionally in dogs.

Escape of the heart from stimulation of the vagus.—The heart when brought to a standstill by stimulation of the vagus soon commences to beat again and quickly reaches a "constant level," as described by Hough‡ for the cat and dog. The time required for this escape to occur and the manner of its occurrence and its extent varied greatly. The most usual mode of escape seemed to be that in which the heart, after remaining at a standstill for a short time, suddenly began to beat at a rate which it maintained as long as the stimulation continued. Sometimes this rate was remarkably slow, as is shown in the following experiment:

Feb. 9. Female opossum, etherized. Heart rate 38½ in 10 seconds; blood pressure 102 mm. Hg. Stimulation of the peripheral end of the left vagus with an induced current of moderate intensity caused complete standstill of the heart for 90 seconds. The heart then began to beat at the rate of 5 in 10 seconds, and continued to beat at this rate as long as the stimulation continued (15 minutes), and for some time afterwards. The blood-pressure curve in this experiment is very interesting; with the first three beats of the heart the pressure rose to 64 mm. Hg, or to considerably more than one-half the normal pressure. It fell to 48 mm.

* Cf. Howell, *Journal of Physiology*, xvi (1894), 304.

† This is true of the guineapig also, as one of us (D. W. H.) has observed.

‡ Hough, *Journal of Physiology*, xviii (1895), 177.

and then rose to 54, at which height it remained during the remainder of the stimulation.

In the above experiment a heart rate of 5 in 10 seconds maintained a blood pressure one-half as great as did a rate of 38½, or nearly eight times as rapid. We shall give later similar instances of the independence of the heart rate and blood pressure.

When the heart was merely slowed by stimulation of the vagus, but not brought to a standstill, a slight escape usually occurred, as was described by Hough for the cat. For example, in one experiment it escaped from 7½ to 10½ beats in 10 seconds, the rate before stimulation having been 26 in 10 seconds. In another case it escaped from 14 to 15 beats in 10 seconds, the vagus having been stimulated when the heart was beating at the rate of 32½ beats in 10 seconds.

After-effect of vagus stimulation.—Perhaps the most marked peculiarity of the effect of stimulating the vagus of the opossum is the fact that the effect upon the heart continues for some time after the stimulation ceases. In the mammals ordinarily used for laboratory purposes and also in the guinea-pig, as one of us (D. W. H.) has observed, the heart after being stopped or slowed by stimulation of the vagus very quickly returns to its normal rate when the stimulation is discontinued; in the dog, in fact, both the heart rate and the blood pressure usually rise considerably above their previous level. In the opossum, however, the return of the heart to the normal rate after stimulation of the vagus is almost always much slower, and we have never observed a secondary acceleration of the heart or a rise of blood pressure. The curve shown in Fig. 1, p. 715, is a good illustration of what usually occurs.

The after-effect varies with the strength of the stimulus, being much more pronounced with a strong than with a weak current. A point of interest is that of two currents of unequal strength, but each of sufficient strength to cause total inhibition, the stronger one causes a longer after-effect. A similar relation between the after-effect upon the heart and the strength of the stimulus is seen when the accelerator nerves are stimulated; of two stimuli, each causing a maximum acceleration, the stronger one causes the longer after-effect.

This after-effect of vagus stimulation is observed when stimuli of very brief duration are employed, so that it can scarcely be attributed to the effect upon the heart of an imperfect supply of blood; besides, as was shown above, the blood pressure usually rises very quickly and sometimes goes above the previous level, although the heart is greatly slowed. Moreover, a local injury to the nerve at the point stimulated, acting as a continuous stimulus, cannot be considered the cause, for cutting off this part of the nerve does not cause the after-effect to disappear. In fact, the long-continued effect upon the heart of vagus stimulation seems to be due to some change in the heart, just as does the long after-effect observed when the accelerators are stimulated.

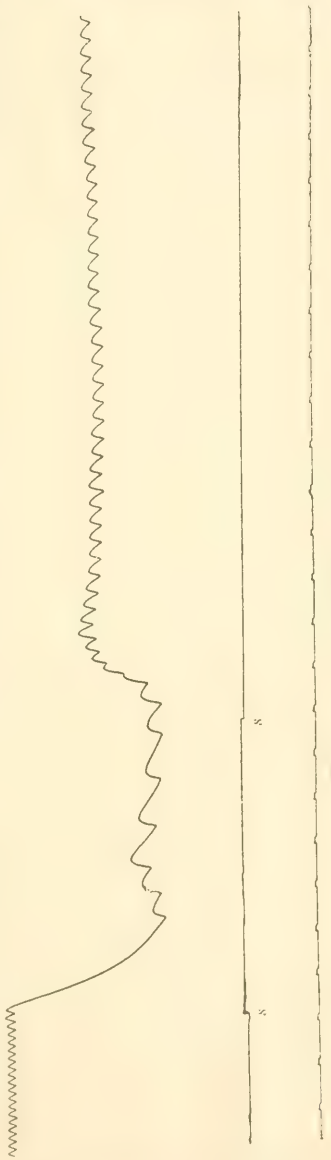


FIG. 1.

Stimulation of the peripheral end of the right vagus (*s-s*); secondary coil 6 cm. from the primary. The pen used to mark the stimulation also wrote the base line. The time is in intervals of 2 seconds. The heart rate before stimulation was 28 in 10 seconds; in the course of one minute after the stimulation had ceased this rate returned. Curve to be read from left to right.

Effect upon the blood pressure of stimulating the peripheral end of the vagus.— One of the most constantly observed peculiarities of the effect of stimulation of the peripheral end of the vagus is the lack of correspondence between the effect upon the heart rate and the blood pressure. The heart may be greatly slowed and yet the blood pressure remain at the previous level or even rise above it.

Thus in one case the heart rate was slowed from 31 to 23 beats in 10 seconds, or 26 per cent, while the blood pressure rose from 127 to 143 mm. Hg. The same thing is even more strikingly shown in Fig. 2.

In this experiment the heart had been completely inhibited by a strong stimulation of the vagus; on weakening the current slightly the heart began to beat at the rate of 16½ beats in 10 seconds and the blood pressure rose above its previous level, when the heart had been beating at the rate of 37½ in 10 seconds.

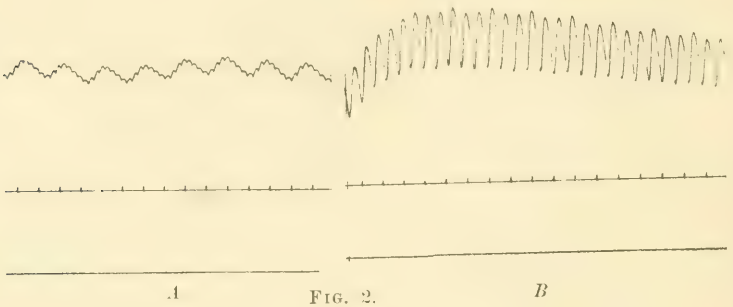


FIG. 2.

Stimulation of the peripheral end of the right vagus. *A* shows the heart rate (37½ beats in 10 seconds) and blood pressure before stimulation. The heart was stopped for several seconds by stimulation of the vagus; the stimulating current was made weaker, the heart began to beat at the rate shown in *B*, and the blood pressure rose and remained at this higher level notwithstanding the slower heart rate. The pleural cavities had been opened and artificial respiration maintained. Time in seconds. Curves to be read from left to right.

That the rise of blood pressure or absence of a fall in these cases is not due to a stimulation of vaso-constrictor nerves, but is due to a direct action upon the heart, is shown by the fact that when atropin is given in sufficient quantity to paralyze the vagus endings, stimulation of the vagus no longer affects the blood pressure. The simplest explanation of this phenomenon appears to us to be that with the slower rate and consequent better filling of the heart the total volume of blood ejected was increased to such an extent that the arterial pressure rose.

These are certainly striking examples of how widely the heart rate

may vary with but slight changes in the blood pressure. A similar phenomenon is frequently observed when the accelerator nerves are stimulated; the heart rate may be greatly accelerated, although the blood pressure is but slightly affected.

3. THE DEPRESSOR NERVE.

We have found a depressor nerve in every opossum but one in which we have looked for it.

Anatomy.—The depressor in the opossum is very similar both anatomically and physiologically to that of the rabbit. It varies somewhat in its origin, but is usually formed by two roots, one from the superior laryngeal nerve and the other from the ganglion of the trunk of the vagus. Sometimes one of these roots seems to be absent the nerve then arising by a single root.

Stimulation of the depressor.—When the central end of one of the depressor nerves is stimulated with the ordinary faradic current, the blood pressure slowly falls until it reaches a certain level, at which it remains as long as the stimulation continues. After the cessation of stimulation the blood pressure slowly returns to its former height; the return seems to occur more quickly after stimulating with a weak than with a strong current, although the fall of pressure was the same (*i. e.* maximal) in both cases. In all cases a longer time was required for the return than for the fall of pressure.

The maximum effect upon the blood pressure may occur after the stimulation has ceased if this is of brief duration. Thus in one experiment the stimulation continued 20 seconds; before the stimulation the blood pressure was 70 mm.; at the end of the first 10 seconds of stimulation it was 56 mm.; at the end of 20 seconds, 44 mm., and 10 seconds after the cessation of stimulation it was 40 mm., from which height it slowly returned to the normal.

Stimulation of the depressor causes a slight reflex slowing of the heart in case the vagi are intact. If the stimulation is continued for some time the heart rate, as well as the blood pressure, remains at a constant level, differing in this respect from the effect in the rabbit, in which animal the effect upon the heart usually disappears very

soon after the stimulation begins. After the stimulation the heart rate seems to return to the normal sooner than does the blood pressure.

The effect upon the respiration of stimulating the depressor nerve varied in the different experiments; in some, respiration seemed to be not at all affected, while in others it was slowed or completely inhibited for a short time. Sometimes, in the same animal, one depressor affected the respiration while the other did not. The effect upon the blood pressure, however, was always the same, whatever the effect upon the respiration.

Comparison of the effect of stimulating the depressor and the central end of the vagus.—Stimulation of the central end of the vagus was usually followed by a fall of blood pressure. This was true whether the other vagus was cut or intact. The fall of blood pressure in these cases, however, differed as a rule from that following stimulation of the central end of the depressor; in the case of the vagus the blood pressure almost always returned to or rose above its previous level during the stimulation, provided that this was somewhat prolonged, whereas with the depressor the blood pressure remained at a uniform low level throughout. A similar difference has been described by Bayliss* in the effects of stimulating the central end of the vagus and of the depressor in the rabbit.

The respiration was inhibited by stimulation of the central end of the vagus, and it seemed possible that the rise of blood pressure during long-continued stimulation of the vagus described above might be due to stimulation of the vaso-constrictor centre by beginning asphyxia. That this explanation will not hold, however, is shown by the fact that sometimes the blood pressure does not rise after the previous fall during the stimulation of one vagus while it does when the other vagus is stimulated, although the respiration was inhibited in both cases.

Sometimes the effect upon the blood pressure of stimulating the central end of one vagus differed from that resulting from stimulation of the central end of the other and both differed from the typical depressor effect. There is nothing to indicate that in these cases the

* Bayliss, *Journal of Physiology*, xiv (1893), 316.

condition of the vaso-motor centre had changed in the intervals between these stimulations; hence the simplest explanation of these various results is that these different nerves contain fibres having different physiological functions, and the effect upon the blood pressure is determined by the nature and number of the fibres stimulated.*

We may suppose, for example, that some of these nerves contain fibres which cause a fall of blood pressure by inhibiting the vaso-constrictor centre, while others excite the vaso-dilator centre.

4. THE ACCELERATOR NERVES.

On the whole our experiments on the accelerator nerves have not been entirely satisfactory; this has been due, in part, to the fact that these nerves are usually surrounded by fat, which makes their preparation very difficult.

Anatomy.—The anatomy of these nerves in the opossum seems to be very similar to that in the other mammals thus far investigated: apparently, however, there are greater individual variations in the opossum. The first three or four thoracic ganglia of the sympathetic chain are usually united to form one large ganglion, the "stellate ganglion"; occasionally, however, these ganglia are united to form two smaller instead of one large ganglion. The stellate ganglion or the ganglion having the same position as the stellate ganglion is united with the inferior cervical ganglion of the sympathetic by two nerve trunks which form a well marked *annulus of Vieussens*, although at times there is but one nerve connecting the ganglia. The *rami communicantes* passing from the lower cervical and upper thoracic spinal nerves form a plexus from which a variable number of branches pass to the stellate ganglion. Frequently two or three small branches pass from each of the spinal nerves in this region to the plexus. The number of branches passing from the plexus to the stellate ganglion is usually four or five. One or two *rami communicantes* join the sympathetic nerve between the stellate ganglion and the first separate thoracic ganglion. Stimulation of the various *rami communicantes*

* Bayliss, *op. cit.*, p. 317; Howell, *op. cit.*, p. 310; Hunt, *Journal of Physiology*, xviii (1895), 402.

between the last cervical and 3rd dorsal nerves inclusive has caused acceleration of the heart, as has also stimulation of the sympathetic below the entrance of the 3rd *ramus communicans.* From the stellate ganglion the accelerator fibres, as shown by stimulation, pass in part to the inferior cervical ganglion through the nerve or nerves (*annulus of Vieussens*) connecting these ganglia, and in part directly towards the heart from the stellate ganglion or in small branches given off from the annulus. In a few animals a comparatively large nerve, evidently corresponding to the "*nervus accelerans*" of the cat, passed from the stellate ganglion directly towards the heart; stimulation of this nerve caused marked acceleration.

Stimulation of the accelerator nerves.—In most respects the effect of stimulating these nerves is the same as in other mammals—an increase in the heart rate, with or without a rise of blood pressure. Perhaps the most interesting point which we have observed is the tendency of the ventricle to beat irregularly when they are stimulated. Very frequently the first effect of the stimulation was to cause a slowing of the rate of the ventricle; this was followed, either during or after the stimulation, by a more rapid but often irregular rate. Judging from what we have seen with great ease in the experiment upon the calf described in the following paper and from less satisfactory observations upon the opossum's heart, we are confident that the slowing and irregularity of the ventricle were due to the ventricle's failing to respond to all the beats of the auricles. Sometimes the ventricular beat followed each auricular beat and at other times only every second or third beat. This irregularity of the ventricle was most marked when strong stimuli were applied to the accelerators; still it occurred also when weak stimuli were applied so that the total effect upon the heart was slight. As a rule after this slow or irregular rate had continued for a variable length of time, it was suddenly replaced by a uniform rapid rate. In other cases the first effect of stimulation was a slight acceleration which soon gave way to the slow or irregular rate as the stimulation continued; after the stimulation the rapid regular rate appeared again. In some cases the acceleration was very considerable, *e. g.* in one experiment there was an increase from 23 to 41½ beats in ten seconds, or an acceleration

of about 80 per cent resulting from the stimulation of the above-mentioned branch of the stellate ganglion ("*nervus accelerans*").

The effect upon blood pressure of stimulating these nerves was variable. As a rule the blood pressure was but little affected even when the acceleration was considerable, resembling in this respect the result so frequently obtained in the dog and cat. Thus in the experiment mentioned above in which there was an acceleration of 80 per cent, there was no change in the blood pressure.

In other respects the effect of stimulating the accelerator nerves in the opossum is similar to that observed in other mammals. Thus a moderately strong stimulus is required for an effect to be produced, and the difference between the strength of a minimal and a maximal stimulus is not great. The latent period is long and there is a long after-effect. Sometimes during the after-effect there is a sudden slowing of the heart rate, although it remains above the normal; from this new rate there is a gradual return to the normal. For example, in one case the rate before stimulation was 23 beats in 10 seconds, soon after stimulation it was 38; it then suddenly changed to 27, from which rate it slowly dropped to 24. We know of no explanation of this peculiarity.

The following figures from one of our experiments are interesting as bearing upon the relation of the inhibiting to the accelerator nerves: First the accelerator nerves were stimulated alone and the heart rate increased from 32 to 38½ beats in 10 seconds (*i. e.* there was an acceleration of 20 per cent). The vagus was now stimulated for some time; the heart rate fell from 33 to 13½ in 10 seconds: during the stimulation of the vagus the accelerators were stimulated again with the same strength of current as before; the rate increased to 20 (*i. e.* there was an acceleration of 48.1 per cent, or a greater acceleration relatively than when the accelerators were stimulated alone).

Obviously the effect in this case of stimulating the two nerves simultaneously was the resultant of the effects of stimulating the nerves separately. This result agrees entirely with what one of us* has found to be the case in experiments upon dogs and cats.

* Hunt, *Journal of Experimental Medicine*, ii (1897), 151.

NOTE ON THE PHYSIOLOGY OF THE CARDIAC NERVES OF THE CALF.

By REID HUNT and D. W. HARRINGTON.

(From the Physiological Laboratory of Columbia University at the College of Physicians and Surgeons, New York.)

We were able to experiment upon but one calf, and had we any expectation of continuing this investigation in the near future we should not publish the results of this experiment at present. Our results, however, seem to us so satisfactory and conclusive that we feel justified in describing them. The heart of the calf is so large and the rate of beat so slow that every change can be followed by the eye with great ease, and the effects of stimulating various nerves can be determined more satisfactorily in some respects than when recording apparatus is applied to the smaller and more rapid hearts of the animals ordinarily used in the laboratory.

The calf upon which we experimented had been used by Dr. Curtis in a lecture demonstration and had been under the influence of ether for some time, but the heart was beating vigorously, and the blood pressure, which was recorded by the mercury manometer in the usual manner, was moderately high (100 mm. of mercury).

Stimulation of the vagus.—Stimulation of the peripheral end of the vagus with currents of moderate intensity caused slowing of both auricle and ventricle. In a number of cases, however, the ventricle was slowed very decidedly, while the rate of the auricle was but slightly affected. This result agrees with that described by Franck* for the dog, but differs from the results obtained by most experimenters for this animal. McWilliam,† Bayliss and Starling,‡ and Roy and Adami,§ for example, speak of the auricles in the dog as being

* Franck, *Archives de Physiologie*, 5. s., ii (1890), 403.
† McWilliam, *Journal of Physiology*, ix (1888), 345.
‡ Bayliss and Starling, *ib.* xiii (1892), 407.
§ Roy and Adami, *Phil. Trans.*, clxxxiii (B), (1892), 199.

Reprinted from the Journal of Experimental Medicine, Vol. II, No. 6.

more easily slowed by stimulation of the vagus than are the ventricles. In none of the several stimulations of the vagus in the calf did we observe a slowing of the auricles without a slowing of the ventricles also.

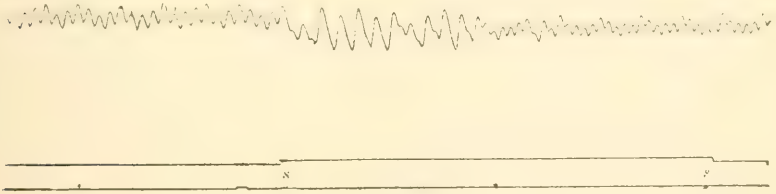
It is interesting to note that sometimes there was an after-effect of the stimulation of the vagus in which the effect upon the ventricle was more marked than that upon the auricles. Thus in one case, after a long-continued stimulation of the vagus, during which auricles and ventricles were both slowed but continued to beat together, the ventricles did not return to their normal rate, while the auricles did return, and it was observed that the ventricles were following at times every auricular beat, and at other times only every second beat. While this slow rate of the ventricles continued, the accelerators were stimulated and the ventricles began at once to follow all the auricular beats. The rate of the auricles, however, was but slightly increased. After the cessation of the stimulation of the accelerators the slow irregular beat of the ventricles returned.

Apparently these results and similar ones obtained in the experiments upon the opossum can be explained satisfactorily by supposing the conductivity of the muscle fibres connecting the auricle and ventricle to have been altered by the stimulation of the nerves.* After the prolonged stimulation of the vagus, the conductivity of these muscle fibres seemed to be depressed for some time; stimulation of the accelerators apparently caused a temporary increase of their irritability, and as a consequence the ventricle followed every auricular beat. So, also, the decreased conductivity of these fibres resulting from the action of the vagus may explain why stimulation of these nerves at times caused a slowing of the ventricles while the auricles were not much affected. Possibly this factor—the changes in the conductivity of the muscle fibres between the auricles and ventricles—has not received sufficient attention from some of the physiologists who have discussed the relative effects of the stimulation of the vagus and accelerator nerves upon the different parts of the heart.

* *Cf.* Gaskell, *Journal of Physiology*, iv (1883), 100; McWilliam, *op. cit.* 367; Bayliss and Starling, *op. cit.* 412.

Stimulation of the peripheral end of the vagus with a very weak current caused in one or two cases a slight acceleration of the heart, as is often observed in the dog.

Accelerator nerves.—We stimulated two nerves passing from the spinal nerves to the stellate ganglion—the *ramus communicans* from the second spinal nerve and a nerve accompanying the vertebral artery (the "*nervus vertebralis*"). Stimulation of both of these nerves caused acceleration of the heart; the results differed, however, in a very interesting manner according as one or the other nerve was stimulated. The immediate effect of stimulating the vertebral nerve was to cause an acceleration of the auricles, but a slowing of the ventricles due to failure of the latter to follow all of the beats of the former. Frequently, if the stimulation was continued for some time, the ventricles began to follow all the auricular beats. We have in this case an illustration of how stimulation of the accelerator nerves can cause an actual slowing of the ventricles—a possibility recently pointed out by Engelmann.* This primary slowing was always obtained whatever the strength of the stimulus used; the acceleration of the auricles and the slowing of the ventricles was most marked, however, with strong stimuli.



Stimulation (*s*-*s*) of the vertebral nerve; the secondary coil was 12 cm. from the primary. In the early part of the stimulation the ventricles failed to follow all the auricular beats, and the result was a slight slowing of the pulse; later there was an acceleration, the ventricles now beating at the same rate as the auricles. Time in intervals of 10 seconds. Curve to be read from left to right.

During the stimulation, the result of which is shown in the accompanying figure, the secondary coil of the induction apparatus was 12 cm. from the primary coil; the rate of the auricles and ventricles

* Engelmann, Pflüger's *Archiv*, lxv (1896), 161.

before stimulation was 20 beats in 10 seconds. In the first 10 seconds during stimulation the auricle gave 24 beats, the ventricle but 19, as it failed to follow all the auricular beats; in the second period of 10 seconds both auricle and ventricle gave 26 beats and the latter followed the former throughout. In a second stimulation the stimulus was stronger, the coil being at 10 cm., before stimulation the auricle and ventricle were beating at the rate of 19½ in 10 seconds; during stimulation the auricles beat at the rate of 26 in 10 seconds, while the ventricles, following only every second auricular beat, had a rate of 13 in 10 seconds. Later the rate of the ventricle became more rapid, following all the auricular beats.

The effect upon the heart of stimulating the 2nd *ramus communicans* differed from the above in that both auricle and ventricle were uniformly accelerated. The following figures give the result of stimulating the 2nd *ramus communicans* with the coil at 10 cm. (the same strength of current as was used in the second of the above stimulations of the vertebral). The rate of both auricle and ventricle before stimulation was 20 in 10 seconds; during the first 10 seconds the rate increased to 23½, during the second 10 seconds it was 28, during the third, 28½, and during the first 10 seconds after stimulation it was 29½. Throughout the stimulation each auricular beat was followed by a ventricular beat, and this occurred also when stimuli of various intensities were used.

The above facts show that in this individual at least the accelerator fibres passing through the vertebral nerve were different from those in the 2nd *ramus communicans*; stimulation of each nerve caused acceleration of the auricle, but the fibres of the 2nd *ramus communicans* evidently had more effect upon the ventricle than did those of the vertebral. This difference may be explained by supposing that the *ramus communicans* contained more fibres passing to the ventricle than did the vertebral nerve, or, and this is perhaps more probable, by supposing that it contained more fibres, stimulation of which caused the conductivity of the muscle fibres connecting the auricles and ventricles to be increased. In any case, it is certain that the accelerator fibres in the two nerves differed in either their ana-

tomical or physiological relations to the heart. Bayliss and Starling* observed a similar separation of the functions of the accelerator fibres in the dog and ascribed the result to the earlier fatigue of one set of fibres; the element of fatigue can probably be excluded from our experiment upon the calf, for both nerves had received the same treatment.

We also tried the effect of stimulating the inhibitory and accelerator nerves simultaneously. The peripheral end of one vagus was stimulated with an induced current produced by the slow interruption of the primary current with the "Schlagwähler"; both auricles and ventricles were slowed. While the stimulation of the vagus was continued the accelerators were stimulated: the rate of both auricles and ventricles was accelerated.

Thus the antagonism of the inhibitory and accelerator nerves, already found to hold in the case of the ventricles of other animals, is found to occur in the calf also, and holds for the auricles as well as for the ventricles.†

* Bayliss and Starling, *op. cit.* p. 416.

† Since the completion of my paper upon the relation of the inhibitory to the accelerator nerves of the heart (*Journal of Experimental Medicine*, ii (1897), 151), I have repeatedly observed directly the effect upon the auricle and ventricle of the simultaneous stimulation of these nerves in the dog. With the strength of current which I used, a ventricular always followed an auricular beat, and in all cases the effect upon the rate of the auricle as well as upon that of the ventricle, was approximately the algebraic sum of the effects produced by stimulating the nerves separately. An "independent ventricular rhythm" which might complicate the results was never caused by the stimulation of the vagus in my experiments.—R. H.

(Studies from the physiological department at Columbia University, College of Physicians and Surgeons, New York. Vol. I.)

Reprinted from the „Archiv für Verdauungskrankheiten", Band III, Heft 2.

Ueber Reizversuche mit Inductionsströmen am Tiermagen.

Eine Antwort auf Dr. M. Einhorn's Kritik nebst Mitteilung einiger Versuchsergebnisse.

Von

S. J. MELTZER

in New-York.

Im zweiten Bande dieses Archivs befindet sich ein Artikel von Herrn Dr. M. Einhorn, betitelt: Einige Experimente über den Einfluss der direkten Magenelektrisation. Der Verfasser sagt darin, dass ich in einer Arbeit[1]) über die Faradisation des Magendarmkanals von Tieren gegen die direkte Elektrisation als therapeutisches Mittel aufgetreten bin. Er habe sich darum veranlasst gesehen, meine Angaben einer Kritik zu unterziehen. Einhorn hat zu diesem Zwecke, so behauptet er, meine Versuche wiederholt und kam ungefähr zu dem Schlusse, dass meine thatsächlichen Angaben unrichtig sind und meine speculativen Schlüsse auf falscher Basis beruhen und dass seine Reizversuche an Tieren die Richtigkeit seiner Auffassung vom Werte der direkten Faradisation des Magens darthun.

Ich will zunächst folgendes bemerken: In meiner Arbeit, auf die Herr Dr. Einhorn Bezug nimmt, habe ich die Resultate meiner Reizversuche in kurz gedrängter Form berichtet, ohne irgend eine Theorie aufzustellen oder irgend einen praktischen Schluss zu ziehen. Um jedes Missverständnis zu vermeiden, habe ich noch ausdrücklich betont, dass meine Resultate nur für die Tiere Giltigkeit haben, an denen die Experimente ausgeführt worden sind. Ich wollte eben nur eine thatsächliche, rein wissenschaftliche Mitteilung machen. Trotz meiner ängstlichen Vorsicht hat dennoch Herr Dr. Einhorn zu meinem Bedauern in meiner Arbeit zu entdecken vermocht, dass ich gegen die direkte Elektrisation als ein therapeutisches Mittel aufgetreten bin. Indessen die Kritik ist einmal da, und wir müssen uns jetzt mit dieser selbst befassen.

[1]) S. J. Meltzer, An Experimental Study of Direct and Indirect Faradization of the Digestive Canal. New-York. Med. Journ. June 15. 1895.

Herr Dr. Einhorn hat in meiner Mitteilung drei befremdliche Punkte gefunden: zwei betrafen Thatsachen und der dritte ist, wie er sagt, eine Theorie. Mit diesen Punkten räumte er kurz auf: Die Theorie sei falsch, und die Thatsachen konnte er nicht bestätigen. Dem gegenüber muss ich hervorheben, dass meine Reizversuche, so weit sie den Magen betrafen, zu folgenden Ergebnissen geführt haben: 1. Inductionsströme veranlassen fast gar keine Contraction am Fundus. 2. Inductionsströme, die stark genug sind, um maximale Contractionen von der Serosa her auszulösen, verursachen gar keine Contraction, wenn sie an die Mucosa angebracht werden. 3. Wenn eine Elektrode auf die Schleimhaut und die andere auf die Serosa in einer Entfernung von etwa 2 cm angelegt werden, bringen starke Ströme gleichfalls keine Contraction hervor. 4. Wenn eine Elektrode auf die Haut in der Magengegend und die andere Elektrode auf den Rücken angelegt oder in das Mageninnere eingeführt wird, so vermögen sogar sehr starke Ströme keine Contraction des Magens zu veranlassen. Ja, durch eine gewisse Versuchsanordnung konnte nachgewiesen werden, dass dabei auf der Serosa kein Strom gefunden werden konnte, der ausgereicht hätte, wenigstens den Ischiadicus des Tieres zu reizen. Es muss doch auf den ersten Blick jedem klar sein, dass, wenn irgend etwas in meiner Mitteilung gegen die therapeutische Anwendung von Inductionsströmen bei Magenkrankheiten gedeutet werden konnte, so ist es dieser letzte, vierte Punkt. Diesen Punkt jedoch erwähnt Einhorn gar nicht. Ich komme später darauf zurück. Ich will auch die eigentümliche Behandlung, welche Herr Einhorn dem Inhalte des zweiten Punktes angedeihen liess, für eine spätere Besprechung belassen. Mein erstes Interesse gilt der Behauptung des Herrn Dr. Einhorn, dass er zwei meiner thatsächlichen Angaben nicht bestätigen könne.

Die eine Angabe betrifft die geringe Contrahierbarkeit des Fundus. Ich sagte in meiner Arbeit, dass am linken Magenabschnitt, den man kurzweg den Fundus nennen durfte, starke Ströme eine kaum wahrnehmbare Contraction veranlassen. Meine Reizversuche sind an vielen Tieren angestellt worden. Ich sage aber ausdrücklich: „Die Resultate sind an allen drei Arten von Tieren (Hunden, Kaninchen und Katzen) verifiziert worden; ich habe jedoch die meisten Versuche an Hunden angestellt, die für unsern Zweck am geeignetsten sind. Der Kaninchenmagen ist für unsere Hauptstudien kein gutes Objekt." Ich habe noch besonders hervorgehoben, dass der Fundus des Katzenmagens recht gut contrahierbar ist. Das allein beweist schon zur Genüge, dass meine Angaben in Bezug auf die verminderte Contrahierbarkeit des Fundus nicht durch Reizungen von solchen Tieren geprüft werden können, an denen ich nicht experimentiert habe. Bei Fröschen habe ich nur die resultatlose Reizung der Mucosa geprüft, sagte aber auch für diesen Versuch: „dieser dickwandige Magen mit seinen kleinen, langsamen Contractionen ist sicherlich kein wünschenswertes Objekt für das Studium

unseres Phaenomens.“ Für die andern Fragen habe ich den Frosch nicht benutzt. Am allerwenigsten ist es mir in den Sinn gekommen, am kleinen, schlauchartigen Magen des Frosches einen scharfen Unterschied zwischen Fundus und Pars pylorica suchen zu wollen. Nun wollen wir uns daraufhin die Versuche von Einhorn ansehen. Von den 18 Experimenten, die er beschreibt, waren zwölf an Fröschen, zwei an Ratten, drei an Kaninchen und ein Experiment an einem Hunde angestellt worden. Vierzehn seiner Experimente (zwölf Frösche und zwei Ratten), kommen für unsere Discussion gar nicht in Betracht, da ich an diesen Tieren nicht experimentiert und also von ihrem Verhalten nichts ausgesagt habe. Es bleiben daher nur vier Experimente übrig (drei Kaninchen und der eine Hund), deren Resultate mit meinen Ergebnissen verglichen werden könnten. Von den drei Kaninchen ist an einem Tiere (7. Experiment) gar nicht erwähnt, ob der Fundus gereizt worden ist. An einem andern Tiere (17. Experiment) heisst es: „Zeitweise kann man keine, zeitweise kann man eine ganz unerhebliche Contraction bemerken.“ Also doch zeitweise keine Contraction! Es muss Einhorn selbst vor diesem Versuche etwas bange geworden sein, da er ihn in seinem englischen Artikel[1]) ausgelassen hat, der sonst Wort für Wort identisch ist mit seinem Artikel in diesem Archiv. Es bleibt demnach nur ein Versuch an einem Kaninchen übrig (6. Experiment), in dem es heisst: „Die ganze Gegend vom Fundus bis zum Pylorus zeigt dasselbe Phänomen“, nämlich „die Einfurchung an beiden Berührungsstellen“. Also im besten Falle hat Einhorn an einem Kaninchen und einem Hunde meine Angaben nicht bestätigen können. Darf jemand auf Grund von solchen vereinzelten Versuchen die Behauptung aufstellen, dass er die Angabe eines Vorgängers nicht bestätigen kann? Nun sage ich noch selbst: „Meine Resultate repräsentieren nur die Regel und schliessen gewiss nicht die Möglichkeit von Ausnahmen aus.“ Nun zieht Einhorn gar den positiven Schluss, „dass an Hunden, Kaninchen, Ratten und Fröschen“ faradische Ströme auch den Fundus des Magens zur Contraction bringen — Hunde und Kaninchen, mit nur einem Hunde und einem Kaninchen zur Verfügung!

Durchmustert man die reichhaltige Litteratur über Experimente am Magen, so entdeckt man, dass sich schon bei manchen Schriftstellern die beiläufig gemachte Angabe befindet, dass der Fundus nur wenig contrahierbar ist. Man kann sie in der Arbeit von Rossbach[2]) finden. Luederitz[3]) sagt: „Am Blindsack war sie (die Contraction) nicht selten recht geringfügig und konnte trotz beträchtlicher Stromstärke ganz ausbleiben.“ Am bestimmtesten hat v. Ziemssen[4]) die geringe Contrahierbarkeit des Fundus hervorgehoben. Ich habe neuerdings den Gegen-

[1]) New-York. Med. Journal, December 12. 1896.
[2]) Rossbach, Deutsch. Archiv f. klin. Med., Bd. 46.
[3]) Luederitz, Pflüger's Archiv, Bd. 49.
[4]) von Ziemssen, Die Elektricität in der Medicin. 1887.

stand nochmal an mehreren Hunden (11) genauer geprüft und werde die Ergebnisse an einer späteren Stelle genauer formulieren. Jetzt will ich nur sagen, dass ausnahmslos an jedem Tiere ein frappanter Unterschied in der Contrahierbarkeit zwischen dem rechten und dem linken Abschnitte des Magens zu constatieren war und dass ferner bei allen untersuchten Tieren am äussersten Ende des Fundus ein grösserer oder kleinerer Abschnitt gefunden worden ist, der auf die stärksten faradischen Ströme mit keiner Contraction reagiert hatte. Um jedoch diesen Abschnitt gut zu Gesicht zu bekommen, muss das linke Magenende samt der Milz ganz aus der Bauchhöhle herausgehoben werden, eine Manipulation, die, wenn ich nach den gegebenen Beschreibungen urteilen darf, von den meisten Untersuchern nicht zur Anwendung gekommen ist. Dies scheint mir namentlich von den paar Versuchen Einhorn's, die für uns in Betracht kommen, zu gelten, da er mit keiner Silbe erwähnt, dass der ganze Fundus samt Milz aus der Bauchhöhle geholt worden ist. Thut man es aber nicht, so bekommt man im besten Falle nur die rechte Hälfte des Fundus zu Gesicht, an der das Haupt-Phänonem lange nicht so deutlich zu constatieren ist, wie an der linken Hälfte. Uebrigens befindet sich auch bei Einhorn in dem Protokoll über den einzigen Versuch an einem Hund, dass die Faradisierung am Fundus nur eine „lokale Einfurchung", in der Pylorusgegend, aber eine „viel intensivere Contraction" hervorgebracht hatte; also auch an diesem Hunde war ein deutlicher Unterschied zwischen Fundus und Pylorus vorhanden! Bei dem einen hierher gehörigen Versuche am Kaninchen, ist von einem Contractionsgrade nicht die Rede, und es konnte sein, dass auch da ein gewisser Unterschied vorhanden war. Uebrigens handelt es sich in diesem Falle um ein nicht gehungertes Kaninchen, der Magen war also, wie gewöhnlich, überfüllt; ein gewiss äusserst ungeeignetes Objekt, daran Vergleichsstudien über die Contractionsfähigkeit gewisser Magenteile anstellen zu wollen.

Einhorn's Behauptung, dass er meine Angabe über die geringe Contrahierbarkeit des Fundus nicht bestätigen konnte, basiert demnach auf zwei Versuchen, an einem Hunde und an einem Kaninchen, deren linke Hälfte des Fundus er wahrscheinlich gar nicht gereizt hatte; und am Hunde hat er selber einen Unterschied zwischen Fundus und Pylorus in seinem Protokolle notiert. Nur an den „Einfurchungen" des gefüllten Magens des Kaninchens hat Einhorn vielleicht keinen Unterschied zwischen den beiden Magenabschnitten bemerkt.

Der andere thatsächliche Punkt bezieht sich auf meine Angabe, dass, wenn eine Elektrode im Magen und die andere auf der Serosa sich befindet, der Magen durch einen starken faradischen Strom nicht zur Contraction gebracht werden kann. Herr Dr. Einhorn sagt, dass seine Versuche meine Angaben nicht bestätigen. Wir wollen uns meine Angabe und seine bezüglichen Versuche näher besehen. — Diese meine Angabe kann

nur im Zusammenhang mit einer andern, vorangegangenen Mitteilung verstanden werden. Ich hatte zuerst festgestellt, dass sogar „starke Ströme", welche von der Serosa aus eine maximale Contraction auslösen, von der Schleimhaut aus keinerlei Contraction zu verursachen vermögen. Daraufhin habe ich weiter festgestellt, dass, wenn sogar nur eine Elektrode auf der Schleimhaut, die andere aber auf der Serosa sich befindet, „starke Ströme" keine Contraction des Magens veranlassen, so lange die Elektroden etwa 2 cm von einander entfernt sind. Ich habe jedoch bereits vorher angegeben, dass „sehr starke Ströme" schliesslich auch von der Schleimhaut aus eine, wenn auch mässige Wirkung hervorbringen. Das gilt selbstverständlich um so mehr für den Fall, wo nur eine Elektrode auf der Schleimhaut, die andere aber auf der Serosa ruhte; ich habe dies doch aber nicht weiter ausgeführt, weil es selbstverständlich war, und weil es sich damals nur um eine knapp gehaltene Mitteilung gehandelt hatte. Was ich unter „starken" und „sehr starken" Strömen verstanden habe, das habe ich doch ganz genau angegeben. Ich habe das grössere der gebräuchlichen Du Bois-Reymond Schlitteninductorien (über 10,000 Windungen) benutzt, das mit einem Grove'schen Elemente bespannt war. Mit „starken Strömen" meinte ich einen Rollenabstand (Ra) von 40 oder 50 (und in manchen Fällen sogar schon 80 oder 90) mm. Jemand, der unter diesen, leicht einzuhaltenen Bedingungen meine Versuche wiederholt hätte, wäre imstande gewesen, über diese ein Urteil zu gewinnen. Besehen wir uns aber Einhorn's Angaben genauer. An keiner Stelle seines Artikels sagt er uns, mit was für Apparaten, mit was für Elementen und mit welchen Stromstärken er gearbeitet hatte. Allgemein findet man darin nur kurzweg: Faradisation; ein paar Mal spricht er von schwachen und ein Mal von mittelstarken Strömen. Welche Stärke er damit meint und wie sie sich mit den von mir benutzten Stromstärken vergleichen liess, das sagt uns der Autor mit keinem Wort. Offenbar liess seine Versuchsanordnung eine solche Messung und Vergleichung gar nicht zu. Er konnte demnach auch gar nicht wissen, ob er meine Angabe widerlegt. — Uebrigens giebt uns Herr Dr. Einhorn unabsichtlich doch einen Fingerzeig darüber, ungefähr wie stark die Ströme waren, die er benutzt hatte. Im zweiten und dritten Experimente heisst es: „Wenn beide Elektroden, in einem Abstand von 5 bis 6 mm, die Schleimhaut des Froschmagens berührten, so entstanden Zuckungen des ganzen Körpers! Nun, solche starken Ströme habe ich gewiss nicht gebraucht und würde ich auch gewiss nicht gebrauchen, wenn ich namentlich lokale Effekte studieren wollte! — Ferner hat Einhorn die meisten seiner Versuche an Fröschen angestellt, an deren Magen es wohl schwer sein dürfte, die Elektroden viel mehr als zwei cm von einander entfernt zu halten! Uebrigens habe ich die in Rede stehenden Versuche nur an Hunden gemacht, und zwar wurde dabei von einer Eröffnung des Magens Abstand genommen, um die Möglichkeit eines Strom-

schlusses zu verhüten, der den kurzen Weg durch Mucosa, Schnitt und Serosa nehmen könnte. Die Elektrode wurde darum stets durchs Maul in den unversehrten Magen gebracht. Einhorn hingegen hat in den Versuchen an den grösseren Tieren die Elektrode in den Magen stets durch eine Oeffnung in denselben eingeführt. — Endlich hat Einhorn an seinem einzigen Versuche am Hunde beim Halten der einen Elektrode im Magen und der andern auf der Serosa gar keine lokale Contraction, sondern „eine leichte Contraction peristaltischen Charakters" gesehen. Ich aber rede nur von einer lokalen Contraction und habe noch ausdrücklich vor einer Verwechselung mit einer zufällig anwesenden peristaltischen Contraction gewarnt.

Es muss demnach für jeden klar genug sein, dass die Behauptung des Herrn Dr. Einhorn, er habe meine beiden thatsächlichen Angaben nicht bestätigt gefunden, völlig haltlos und ohne genügende Selbstkritik aufgestellt worden ist.

Von einer dritten von mir gemachten Angabe behauptet Einhorn, dass sie nur eine Theorie enthält und nicht richtig ist. Das bezieht sich auf meinen Satz, dass die Schleimhaut des Magens die Fähigkeit besitzt, dem Durchdringen von faradischen Strömen nach der Muscularis hin einen Widerstand entgegenzusetzen. Die Behandlung, welche Herr Dr. Einhorn diesem Punkte angedeihen liess, ist eine etwas eigentümliche. In meiner damaligen Arbeit habe ich auf die Beobachtung, dass man mit starken faradischen Strömen von der Schleimhaut aus keine Contractionen auslösen kann, das grösste Gewicht gelegt. Man kann z. B. im Oesophagus, noch oberhalb der Cardia, mit allen Stromstärken, die eine Contraction von der Serosa aus hervorzubringen vermögen, auch eine entschiedene Contraction von der Schleimhaut aus veranlassen. Im Magen aber gelingt es nicht, sogar mit recht starken Strömen auch nur eine Andeutung von einer Contraction hervorzubringen. Diese Beobachtung scheint in der That ganz neu zu sein. — Ich habe in der ganzen Arbeit jede Erklärung für diese Thatsache vermieden. Wohl habe ich ein paar Mal vom „Widerstande" der Schleimhaut gesprochen, habe es aber nur gethan, um einen kurzen Ausdruck zu gebrauchen, und habe ausdrücklich betont, dass ich eine Erklärung über die Natur dieses Widerstandes zunächst gar nicht versuchen würde, da ich mir eine solche Erklärung für spätere Studien zu reservieren gedachte. — Einhorn leugnet nun die Richtigkeit der Thatsache selbst nicht. Er notiert sie vielmehr selbst in seinen Versuchen und führt sie auch in seinen Schlusssätzen an, obschon in sehr verwässerter Form. Nur deutete er an keiner Stelle an, dass ich es war, der die thatsächliche Beobachtung gemacht hatte. Was er aber mir zuschreibt, ist die Aufstellung einer Theorie neben diesen Punkt, und einer solchen Theorie, die er für falsch hält. — Glaubt denn Einhorn, dass, wenn ich die Absicht hätte, eine Theorie aufzustellen, ich dies nicht ausdrücklich thun, sondern mich nur auf den Gebrauch eines einzigen Wortes verlassen würde? —

Dazu noch eine solche Behauptung aufzustellen angesichts einer ausdrücklichen Verwahrung gegen eine solche Unterschiebung! — Wir wollen uns indessen die Gründe ansehen, warum Herr Dr. Einhorn „meine Theorie“ für falsch hält. Da heisst es bei Einhorn: „Meltzer erklärt dieses Phänomen dadurch, dass der Strom durch die Schleimhaut nicht gut hindurchgehen kann, und dass daher die Magenmuscularis nicht genügend gereizt wird. Es ist aber viel wahrscheinlicher und naheliegender, anzunehmen, dass die Magenmucosa sehr gut leitet und dass eben deswegen der Strom durch die Mucosa allein läuft und die Muscularis nicht erreicht. Der Strom sucht ja immer den kürzesten Weg, auf dem sich der geringste Widerstand befindet.“ Ganz gewiss. Wenn aber für die Leitung in der Richtung der Schleimhautoberfläche der Strom einen verminderten Widerstand findet, so folgt ja daraus, dass in der Richtung durch die Schleimhautdicke, nach der Muscularis hin, die Stromesleitung auf einen vermehrten Widerstand stösst. Wo liegt da ein Widerspruch zwischen Einhorn's Erklärung und „meiner Theorie“? Ich habe nur gesagt, dass der Strom beim Versuche, die Schleimhautdicke zu durchdringen, um an die Muscularis zu gelangen, auf einen vermehrten Widerstand stösst; das war einfach eine Umschreibung der beobachteten Thatsache. Nun kann man diesen „vermehrten Widerstand“ unter anderm auch dadurch erklären, dass die Schleimhautoberfläche vorzüglich gut leitet, sodass der Strom sich lieber nach der Fläche hin als durch die Dicke ausbreitet. Das habe ich selber sehr wohl gewusst, habe aber ausdrücklich betont, dass ich damals keine Erklärung geben wollte.

Wenn Herr Dr. Einhorn nicht durch einen unnötigen Uebereifer befangen gewesen wäre, so würde er das klarliegende Verhältnis nicht missverstanden haben. — Die wirkliche Sachlage ist folgende. Ich habe gefunden, dass faradische Ströme von der Schleimhaut des Magens aus viel schwerer an die Muscularis gelangen, auf einen „vermehrten Widerstand“ stossen, als wir ihn beim Durchtritt von Strömen von andern Schleimhäuten zu den bezüglichen Muskellagen finden. Nun könnte dies dadurch erklärt werden, erstens, dass die Dickenleitung bei allen Schleimhäuten zwar dieselbe ist, dass aber die Flächenleitung auf der Magenschleimhaut besser ist als auf den andern Schleimhäuten. Oder zweitens, dass die Flächenleitung bei allen Schleimhäuten gleich gut ist, dass aber die Dickenleitung bei der Magenmucosa schlechter ist als bei andern Schleimhäuten, vielleicht infolge von grösserer Dicke oder complicierterer Schichtenbildung oder Drüseneinlagerung u. s. w. Es könnte auch sein, dass die sauere Reaction mit der Sache etwas zu thun hat, oder vielleicht ist gar die besondere Anordnung der Submucosa daran Schuld u. s. w. Eine Auswahl zwischen all diesen Möglichkeiten wollte ich nicht durch a prioristische Annahmen treffen, da diese Fragen recht wohl dem Experimente zugänglich sind. Wohl verfüge ich jetzt schon über einige experimentelle Thatsachen, die auf

eine gewisse Lösung hindeuten, sie sind aber lange noch nicht zahlreich und eindeutig genug, um schon jetzt die Fällung eines definitiven Urteils zu gestatten. Ich möchte eben durchaus nicht dem Beispiel des Herrn Dr. Einhorn folgen, der seine Schlüsse von Versuchen zieht, die er an einem Kaninchen, an einem Hunde oder an einem Morris S. angestellt hatte.

Einhorn hat seine Experimente unternommen und seinen Artikel geschrieben, weil, wie er selbst angiebt, ich „gegen die Magen-Elektrisation als therapeutisches Agens aufgetreten bin"; sein Hauptbestreben war daher zu beweisen, dass ich im Unrechte war und demnach indirekte Faradisation ein sehr gutes Mittel ist und bleibt. Dem entsprechend giebt er auch an, dass seine Versuche in der That dargethan haben, dass, „wenn eine Elektrode im Magen ist, die andere an einem nicht zu sehr entfernten Körperteile liegt, so kann man, falls man einen mittelstarken faradischen Strom für 20 bis 30 Sekunden durchgehen lässt, peristaltische Contractionen des Magens beobachten". Aus welchen seiner Versuche mag wohl Einhorn diesen seinen Schluss gezogen haben? Gesetzt den Fall, es sei ihm wirklich gelungen, seine Behauptung zu beweisen, dass er meine Angaben widerlegt hat: was haben jene Behauptungen aber mit diesem Schlusse zu thun? Dass der Fundus sich ebenso contrahiert wie der Pylorus, oder dass „meine Theorie" vom vermehrten Widerstande absolut falsch sei, hat doch sicherlich nichts mit der in diesem Schlusse enthaltenen Frage zu thun. Es hat aber den Anschein, dass Einhorn diesen Schluss in der That aus seinen Versuchen zu ziehen sich für berechtigt hält, welche er über die Reizung mit einer Elektrode auf der Mucosa und der andern auf der Serosa angestellt hatte. Nun sagt er aber in diesem Schlusse, dass der Magen sich peristaltisch contrahierte, während er in nur einem von allen 18 Versuchen (bei Reizung mit einer Elektrode im Magen und der andern auf der Serosa) peristaltische Contractionen verzeichnet. In allen übrigen aber spricht er nur von lokalen Contractionen. Aber abgesehen davon, was haben Versuche, bei denen die eine Elektrode auf der Serosa liegt, mit jenem Schlusse zu thun, der sich auf eine solche Faradisation bezieht, bei der die eine Elektrode auf die Bauchdecke aufgesetzt wird? Ich habe doch nachgewiesen, wie schon oben erwähnt, dass, wenn eine Elektrode im Magen und die andere auf der Bauchdecke oberhalb des Magens liegt, dieser sich durchaus nicht contrahiert. Wenn etwas in meiner Arbeit gegen die therapeutische Anwendung der Faradisation gedeutet werden könnte, so wäre es doch sicherlich dieser Nachweis. Eben diese Versuche hätte Einhorn zu entkräften suchen müssen. Aber weder erwähnt Einhorn, dass ich solche Versuche beschreibe, noch sagt er uns, dass er entsprechende Versuche angestellt hat, die meine Versuche widerlegen, und zieht dennoch aus irgend unerfindlichen Experimenten einen Schluss, der meiner Angabe schnurstracks zuwiderläuft! Am auffälligsten jedoch ist folgendes: Da heisst

es bei Einhorn im ersten Experimente: „Frosch . . . Faradisation . . . die eine Elektrode im Magen . . . berührt die äussere Elektrode dagegen irgend einen Körperteil (Bein oder Bauchdecken), so gerät derselbe in Contraction, während man am Magen nichts wahrnimmt.“ Eine ungefähr ähnliche Angabe findet man auch im 15. Experiment. Also eine Elektrode war im Magen und die andere auf der Bauchdecke, und dennoch vermochte Faradisation keine Bewegung des Magens zu veranlassen. Trotz dieser seiner eigenen unzweideutigen Beobachtungen sagt dennoch Herr Dr. Einhorn, seine Versuche hätten dargethan, dass, wenn eine Elektrode im Magen, die andere auf den Bauchdecken u. s. w. liegt, Faradisation eine Peristaltik des Magens veranlasst.

Herr Dr. Einhorn hat nicht nur meine Angaben nicht widerlegt, sondern zog auch seine anderen Schlüsse aus seinen Experimenten in recht willkürlicher Weise.

Jetzt noch ein Wort zu der ganz willkürlichen Behauptung des Herrn Dr. Einhorn, dass „ich gegen die Magenelektrisation als therapeutisches Agens aufgetreten bin.“ Ich habe aus meinen Versuchen nur den Schluss gezogen, dass sowohl bei der percutanen als auch bei der sogenannten direkten Faradisation des Magens eine Contraction desselben nicht zustande kommt, und habe ausdrücklich zugefügt, dass dieser Schluss nur für die Tiere Gültigkeit hat, an denen meine Experimente angestellt worden waren. Ob bei der therapeutischen Anwendung der Faradisation der menschliche Magen sich contrahiere oder nicht, dies habe ich weiter gar nicht erörtert. Ich habe nur bemerkt, dass die Magenchirurgie eine Gelegenheit bieten könnte, die Befunde, welche ich am Tiermagen gewonnen habe, auf ihre Gültigkeit für den menschlichen Magen zu prüfen. Eher hatte Herr Dr. Einhorn Veranlassung, sich mit Prof. Moritz[1]) abzufinden, der aus seinen Versuchen über die Veränderungen des „inneren Magendruckes“ den Schluss gezogen hat, dass die direkte Faradisation den menschlichen Magen zu keiner Contraction veranlasst. Noch unangenehmer musste ferner Herr Dr. Einhorn sich berührt fühlen von Goldschmidt's[2]) Angaben, nach denen weder der faradische noch der galvanische Strom den menschlichen Magen zur Contraction oder zur Secretion veranlasst! Dabei sagt Goldschmidt gar, dass Einhorn's thatsächliche Angaben seine (Einhorn's) Schlüsse nicht rechtfertigen! — Freilich sagt Goldschmidt dies alles nur im „physiologischen Teil“ seiner Arbeit. Im klinischen Teil erzählt er einfach von vielen Besserungen und Heilungen, welche die Magenelektrisation erzielt hatte! Jemand darf also der Magenelektrisation jeden physiologischen Einfluss absprechen und kann dennoch an deren therapeutische Wirkung glauben. Warum denn dieser Eifer gerade gegen meine rein physiologischen Angaben?

[1]) Moritz, Zeitschrift für Biologie, Bd. 32.
[2]) Goldschmidt, Deutsch. Arch. f. klin. Med., Bd. 56.

Meine Versuche sind im Winter 1894 95 angestellt worden. Ich bin zu den direkten Reizungen des Magendarmkanals nicht etwa durch therapeutische Erwägungen veranlasst worden, sondern bin rein zufällig dazu gekommen im Verlaufe von Versuchen, die ich über die Wirkungen der peripheren Vagusreizung auf den Magen angestellt habe. Die letzteren Versuche habe ich in diesem Winter nochmals aufgenommen und dabei gleichfalls die früher mitgeteilten Befunde durch neue Versuche controlliert. Einen Teil dieser Versuche, namentlich die von Einhorn angezweifelten Punkte, habe ich in der diesjährigen Versammlung der American Physiological Society (29. December 1896) im Physiologischen Laboratorium des Harvard Medical College in Boston (Prof. H. P. Bowditch) an einem Hunde demonstriert, worüber sich in der Wochenschrift „Science" (22. Januar 1897) ein ganz kurzer Bericht befindet. Im folgenden werde ich einige der bis jetzt gewonnenen Ergebnisse hier kurz referieren. Die Versuche sind an (11) Hunden angestellt worden.

Die Reizversuche an der Magenschleimhaut sind oft wiederholt worden, und die Resultate sind jetzt noch prägnanter als früher hervorgetreten. Von jeder Stelle der gesamten Magenmucosa konnte man mit starken faradischen Strömen keine Contraction hervorbringen. Bei sieben Hunden war dies sogar bei 0-Rollenabstand der Fall: bei zwei Hunden trat bei 0-Rollenabstand und bei zwei andern bei 40(mm)-Rollenabstand doch eine mässige Contraction der Pars pylorica ein, während bei Reizungen von der Serosa aus schon Ströme von 130 bis 120 Ra bei allen Tieren eine maximale Contraction hervorzubringen vermochten. Am Oesophagus, sogar in der Nähe der Cardia konnte jede Stromstärke, die ausreicht, eine Contraction von der Serosa hervorzurufen, auch von der Schleimhaut aus eine Contraction auslösen. Uebrigens sind die Elektroden dies Mal nicht durch eine Oeffnung im Magen, sondern durch eine solche im Duodenum in den Magen eingeführt worden. — Benutzt wurde auch diesmal der grosse Du Bois Reymond-Schlitten, der von einer elektrischen Lampe gespeist wurde, die nur wenig stärker als ein Grove'sches Element war. — Wenn eine Elektrode im Magen und die andere auf der Serosa war, so konnte auch diesmal bei ziemlich starken Strömen (etwa 100 Ra) keine Contraction hervorgerufen werden. Bei sehr starken Strömen jedoch (30 bis 40 Ra) trat schliesslich eine Contraction ein. Uebrigens hat diese Reizanordnung weder ein praktisches noch ein physiologisches Interesse, und habe ich auch der Sache nicht viel Aufmerksamkeit geschenkt.

Dass aber eine solche Reizanordnung, bei der eine Elektrode im Magen und die andere auf den Bauchdecken zu liegen kommt, der Magen sich auch bei sehr starken Strömen (0-Ra) durchaus nicht contrahiert, habe ich auch diesmal öfters bestätigen können. Ich will übrigens hier einschaltend bemerken, dass, wenn man auf die Serosa des Magens die Muskelhaut des Oesophagus legt

und dann beide Elektroden auf diese Haut setzt, so bringt kein starker Strom den darunterliegenden Magenteil zur Contraction, während die Muskelhaut des Oesophagus natürlich, sich stark um beide Pole contrahiert. Diese Haut ist eben ein sehr guter Leiter und erlaubt gar keine Stromabzweigung zu der darunterliegenden Magenmuskulatur. Dasselbe gilt wohl auch für die Körpermuskulatur, die wahrscheinlich nur selten das Durchdringen eines faradischen Stromes zu den darunterliegenden Geweben gestattet.

Bei keinem der untersuchten Hunde habe ich bis jetzt eine Contraction des Magens auf Vagusreizung vermisst. In einem Tier war nur der rechte, in einem andern Tiere nur der linke Vagus wirksam; bei allen übrigen Hunden waren beide Vagi wirksam, obschon stets in ungleicher Weise entweder in Bezug auf die Erregbarkeit oder auch in Bezug auf die Intensität oder Extensität des Effekts. Curare beeinträchtigt die Wirksamkeit der Vagusreizung beträchtlich. Schwache Reizungen veranlassten manchmal nur eine schwache peristaltische Bewegung, die man jedoch nur selten nach Willkür auslösen konnte. Starke Reizungen veranlassten stets eine heftige simultane Contraction eines ganzen Magenabschnittes; das Nachlassen der Contraction geschah nicht simultan, es bot vielmehr ein Bild einer ablaufenden peristaltischen Welle dar. Stets ging der Wirkung ein langes Latenz-Stadium voraus; auch wurde die Hauptwirkung erst nach Aufhören der Reizung entfaltet. Auf die sehr interessanten Einzelheiten dieses Phänomens soll hier nicht eingegangen werden. Was ich jedoch an dieser Stelle besonders hervorheben will, ist folgendes:

Mochten die Nerven noch so erregbar und die Reizung noch so stark und anhaltend sein, die Contraction blieb stets beschränkt auf die rechte Magenhälfte! Hat man im Fundus eine Oeffnung angebracht, durch welche alle Luft und Flüssigkeit entweichen konnte, so hat man bald beobachten können, wie neben der strangförmigen Contraction des rechten Magenabschnittes der linke Abschnitt ganz erschlafft wie ein Sack dalag. Je geringer die Nervenerregbarkeit, je schwächer der Reiz war und je kürzer er dauerte, desto kleiner war der sich contrahierende rechte Abschnitt.

Ich habe jetzt bereits eine ziemlich grosse Zahl von Hundemagen zu beobachten Gelegenheit gehabt. Eine spontane Peristaltik am Magen war durchaus kein häufiges Ereignis, jedenfalls nicht so häufig, wie es von vielen Autoren angegeben wird. Meine Tiere waren jedoch stets in tiefer Narkose, welcher Umstand vielleicht die Seltenheit des Auftretens der Peristaltik erklären mag. Es ist mir manchmal gelungen, eine bald vorübergehende Peristaltik hervorzurufen: durch mechanische Reize (Druck oder Stich); durch chemische Reize (Kali- oder Natron-Salze); durch thermische Reize (Kälte oder Hitze) und endlich auch, und am besten, durch Asphyxie. Alle diese Reize sind

durchaus unverlässlich und schlugen nur in der Minorität der Versuche an. Ich habe aber seit langer Zeit stets auf den Ort am Magen geachtet, wo die Peristaltik aufzutreten pflegt, und ich kann jetzt meine Beobachtungen kurz dahin zusammenfassen, dass ich weder die spontane Peristaltik noch solche peristaltischen Bewegungen, welche durch mechanische, chemische, thermische oder elektrische Reize oder durch Asphyxie hervorgerufen werden, jemals am linken Abschnitte (etwa am letzten Drittel) entstehen und ablaufen gesehen habe.

Die Frage nach der lokalen Contractilität des Magens habe ich gleichfalls nachuntersucht, und zwar mit Inductionsströmen von verschiedensten Intensitäten. Im allgemeinen ergab auch die jetzige Untersuchung einen scharfen, unzweideutigen Unterschied in der Contractilität zwischen dem rechten und dem linken Magenabschnitt. Mit mässig starken Strömen (10—30 Ra) kann man nur an der pars pylorica allein eine energische örtliche Contraction erzielen. Bei Verstärkungen des Stroms kann man jedoch noch weiter nach links liegende Teile zur Contraction bringen, die zwar um so ausgesprochener wird, je stärker der Strom ist, doch niemals die Intensität, den Grad erreicht, den man am Pylorusteile schon mit relativ mässigen Strömen erzielen kann. Indessen blieb bei allen Tieren am linken Ende des Magens ein Teil übrig, der durch keine Stromstärke, auch nicht bei 0-Ra zu einer Contraction zu bringen war. Bei einigen Hunden war nur um die Elektroden herum ein ganz geringes oberflächliches Runzeln zu bemerken, bei den übrigen Tieren war auch das nicht vorhanden. Für die Magencontractilität stellt das linke Ende einen negativen Pol dar, der durch keine Reizstärke zu bringen ist, während das rechte Ende einen positiven Pol darstellt, an dem schon ein geringer Reiz eine maximale Contraction erzielen kann. Beim Uebergange vom positiven zum negativen Pole findet zunächst eine Abnahme in der Intensität der Contraction statt, d. h. bei gleichbleibender Stromstärke wird die Contractionsgrösse der nach links liegenden Teile des Magens stets geringer und geringer. Eine Stromverstärkung vergrössert zunächst die Contraction der erregbaren Teile und dann macht sie noch weitere, nach links liegende Partien des Magens der Contraction zugänglich. Intensität und Extensität der Contractionen nehmen indessen trotz weiterer Stromverstärkung mehr und mehr ab, bis beide am linken Pole gleich Null werden. — Die lokale Contrahierbarkeit des Magens dehnt sich etwas weiter nach links aus, als die peristaltischen Bewegungen oder die durch Vagusreizungen ausgelösten Contractionen es thun.

Eine wirksame, Nutzen bringende Contraction habe ich an den äussern zwei Drittel des Fundus niemals beobachtet, weder bei den direkten faradischen Reizungen noch bei den indirekten Reizungen vermittelst des Vagus noch bei den spontanen oder durch allerlei Reize ausgelösten peristaltischen Bewegungen.

STUDIES FROM THE DEPARTMENT OF PHYSIOLOGY OF COLUMBIA UNIVERSITY, AT THE COLLEGE OF PHYSICIANS AND SURGEONS OF NEW YORK. VOL. I.

[*Reprinted from The Journal of Experimental Medicine, Vol. II, No. 5.*]

A FURTHER EXPERIMENTAL CONTRIBUTION TO THE KNOWLEDGE OF THE MECHANISM OF DEGLUTITION.

By S. J. MELTZER, M. D.

It is now about seventeen years since Kronecker and myself* advanced the view that in the act of deglutition liquids and semi-solids are not carried down the œsophagus by the slow process of peristalsis, but are thrown down with great rapidity by the energetic contractions of the mylo-hyoid muscles especially. We supported this view, first, by experimental proofs obtained by the graphic method. A rubber balloon which was placed in the œsophagus recorded on a rotating drum two impressions during each single act of deglutition; a short one at the very beginning of the act, and a longer one which appeared the later the deeper the balloon was located within the œsophagus. There could be no doubt that the second impression was brought about by the peristaltic contractions of the œsophagus, while we had abundant reasons to interpret the first impression as coming from the rapid passing of the liquid.

But to obtain a still more striking proof of the rapidity with which the swallowed mass is usually shot down, another experiment was

* Meltzer, Ueber die Vorgänge beim Schlucken. Du Bois-Reymond's *Archiv*, 1880, 446.

made. A stomach tube was introduced into the œsophagus, the lower end with the side openings remaining a few centimetres above the cardia. Inside the tube opposite the side openings a small roll of blue litmus paper was placed with a long thread attached to it, the outer end of the thread projecting from the outside opening of the tube. When the litmus paper was rapidly withdrawn from the tube about half a second after swallowing lemonade, it was found to have turned red. This could only mean that half a second after the beginning of the act of deglutition the acid liquid was in a deep portion of the œsophagus, while the peristalsis, as we knew from our other experiments, could not reach this spot before six seconds.

Although our experiments thus far proved only that the liquid thrown down reaches the lowest segment of the œsophagus quickly, we assumed that it passes at once into the stomach. We were supported in this assumption by our observation that in the rabbit the cardia becomes momentarily relaxed at the very beginning of the deglutition, which would seem to facilitate the entrance of the swallowed mass into the stomach. Later on, however, we modified this view, when I* discovered that in the vast majority of normal individuals, about seven seconds after the beginning of a single act of swallowing, a murmur is to be heard in the region of the cardia, which has the character of a sound produced by liquid and air squeezed through a narrow aperture, while in a minority of individuals at about the beginning of the deglutition a murmur appears in the same region with a character reminding one of a sound caused by pouring or squirting liquid. I have named the former the "squeezing murmur" (*Durchpressgeräusch*) and the latter rare sound the "squirting murmur" (*Durchspritzgeräusch*). We† then took the stand that the mass thrown down is detained in the œsophagus above the cardia until the contraction of the lower section of the œsophagus begins, which occurs according to our experiments about six or seven seconds after the beginning of deglutition and with which the squeezing murmur coin-

* Meltzer, Ueber Schluckgeräusche, *Centralbl. f. d. med. Wissenschaft.*, 1883, No. 1.

† Kronecker and Meltzer, Der Schluckmechanismus u. s. w. Du Bois-Reymond's *Archiv*, 1883, Supplementband.

cides in time. We explained the origin of the sound by assuming that the contraction of the lowest section of the œsophagus squeezes the detained swallowed mass through the tonically contracted cardia, thus producing irregular vibrations which the auscultating ear perceives as a squeezing murmur. The squirting murmur occurs, we assume, in persons whose cardia for some reason or other is relaxed and in whom the swallowed mass is squirted directly into the stomach without any delay.

Our interpretation of the squeezing murmur has met with objections from several writers. Zenker* has put forward the theory that after the arrival of the swallowed mass at the cardia the air becomes separated from the liquid and remains above it, and the liquid soon oozes down noiselessly into the stomach, while the air follows later with a murmur. Why the air should follow regularly after seven seconds Zenker fails to explain, as he was not aware of the presence of the peristalsis just at this time. The theory of Zenker was accepted by Ewald† and by Quincke,‡ with the additional explanation that the air is carried into the stomach by the peristaltic wave which arrives at the lower end of the œsophagus about seven seconds after the beginning of the act of deglutition, a fact which was established by our experiments. But while Zenker's main objection to our statement was based upon the erroneous supposition that we believed the liquid to be thrown down directly into the stomach at the very beginning of the deglutition, the objection of Ewald and Quincke, on the contrary, was directed against the supposition that the liquid is carried down into the stomach by the peristaltic wave only. Both these writers have made some experiments in support of their view. I shall not enter into a detailed analysis of their statements. It suffices to say that the main object of their experiments was to show that the presence of a squeezing murmur depends upon the passing of air through the cardia and that the passage of liquid alone does not produce any sound. From this supposed fact they drew the conclusion that the

* Zenker, *Berliner klin. Wochenschr.*, 1884, p. 38.

† C. A. Ewald, Du Bois-Reymond's *Archiv*, 1886, p. 376.

‡ Quincke, *Arch. f. exp. Path. u. Pharmakol.*, xxii, p. 385, 1887.

peristalsis carries down into the stomach air only, which causes the squeezing murmur, while the liquid oozes noiselessly through the cardia before the arrival of the peristalsis at the lower end of the œsophagus. But as Quincke himself has established the fact that a murmur is present when air and liquid together are passing through the cardia, and as he insists also that air is swallowed in each act of deglutition, it is evident that their experiments are by no means conclusive for their assumption; they rather permit also the theory that the liquid remains above the cardia until the peristalsis carries liquid and air together through the aperture into the stomach, which, according to Quincke, produces a squeezing murmur. We can fully agree with Quincke that each and every act of deglutition also carries air into the stomach, and we have never insisted that the murmur is due to the passage of the liquid alone through the cardia. We have simply stated that the murmur is coincident with the contraction of the lowest segment of the œsophagus and is apparently due to the passage of the swallowed mass through the cardiac orifice, and I am willing to concede now that the presence of air in the swallowed mass is possibly the main factor in the causation of the characteristic squeezing murmur.

The interpretation of the squeezing sound and its origin are, after all, matters of only secondary importance; the main point of physiological interest is the question: Does the liquid thrown down remain above the cardia until the peristalsis carries it into the stomach, or does it ooze down previously to the arrival of the peristalsis? That it makes a halt above the cardia and is not thrown directly into the stomach just after it is squirted down the œsophagus is disputed by hardly any writer, although there is no other proof for this assumption than the presence of the squeezing murmur with its disputed interpretation.

Briefly recapitulated, the present state of the question is as follows: Our positive experiments have proven only that the fluid is squirted down into a deep part of the œsophagus. We may add here that Hamburger's deglutition murmur, which is to be heard at the back alongside the spinal column at about the beginning of the act of de-

glutition, can be followed down only to the eighth dorsal vertebra, which corresponds to a point in the œsophagus a few centimetres above the cardia. As to the further fate of the swallowed mass we have for the present no other information than the presence of a squeezing murmur at the region of the cardia just at the time of the arrival of the peristalsis. We interpreted this murmur as indicating the passage of the entire swallowed mass, air and liquid, into the stomach; the other three writers mentioned ascribe the murmur to the passage of air alone, while they assume that the liquid enters the stomach before the arrival of the peristalsis. It must be admitted, however, that neither of these views is supported by indisputable experimental proof. It is the object of this paper to offer such experimental observations as will, I believe, fully justify the stand which Kronecker and myself have taken in this question.

The observations were made on dogs and rabbits. The dogs were anæsthetized by ether and the rabbits by chloral. The main difficulty in studying deglutition in dogs lay in the strong interference of the etherization with the reflex act of deglutition. In a future communication I intend to report some observations bearing upon this point. Here, however, I shall only state briefly the method which I found to be most suitable for my purpose. After bringing the dog under thorough anæsthesia both superior laryngeal nerves were tied, tracheotomy performed, the larynx well packed with cotton and artificial respiration begun. Now the anæsthesia was reduced to that degree which permitted the return of the deglutition reflex. The state of apnœa which was brought about by the artificial respiration permits a considerable reduction of the etherization. The acts of deglutition were induced either by injecting liquid (water or milk) into the mouth or pharynx, or by faradic stimulation of the central end of one of the superior laryngeal nerves.

My first effort was directed towards getting a full view of the cardiac opening of the stomach during the act of deglutition. For this purpose the stomach of the dog was exposed, a vertical incision of about two inches made and the contents of the stomach removed. Then a wide tube with a reflecting inner surface, a vaginal speculum,

was introduced and so adjusted as to have the cardiac aperture just at the bottom of the tube. An electric light thrown into the tube facilitated the observation greatly, and the escape from the cardiac orifice of liquid or air or both could be easily scrutinized.

We knew from our former experiments that the time which passes from the beginning of the act of deglutition until the peristaltic wave reaches the cardia amounts in dogs to about four seconds. The present task was simply this: To see whether any of the swallowed liquid comes down through the cardiac orifice either abruptly at about the beginning of the act of deglutition or by slow oozing into the stomach before the peristalsis reaches there; or whether the entire swallowed mass comes down through the cardia into the stomach all at once with the peristaltic wave.

The observations were made in the first place by the graphic method, *i. e.*, one observer caused the marking of a lever upon a revolving tambour just at the beginning of the deglutition, which is easily recognizable by the characteristic sharp ascent of the larynx, while another observer, looking into the tube, marked the first appearance of liquid through the cardiac aperture. Or one observer simply called out the beginning of the deglutition and the other called out the appearance of the liquid, the length of the interval being established by a watch or simply by estimation. I have made a series of these observations on many dogs, and on each dog I made numerous single observations, and I can now state that not in one single instance was any liquid projected through the cardia at the beginning of the deglutition or did any ooze through the cardia into the stomach before the arrival of the peristaltic wave. In all cases the swallowed mass was squeezed through the cardia by the peristaltic wave, about four seconds after the beginning of the act of deglutition. When the deglutition was caused by liquid injected into the pharynx the swallowed mass consisted mainly of liquid containing only a few bubbles of air; when caused by stimulation of the laryngeal nerve the mass consisted mainly of air with only a little fluid.

A similar condition I have discovered also in rabbits. The observation is here quite simple and easy. When the stomach is lifted out

from the abdominal cavity, incised, and some of the contents removed from the region of the cardia, the cardiac aperture is plainly exposed to full view. The time for the arrival of the peristalsis at the stomach is in rabbits quite short, being a little less than two seconds. Nevertheless there could be no doubt of the fact that here, too, the swallowed mass reaches the stomach only with the peristalsis.

This line of observation led me to a search as to the exact location of the point where the swallowed mass is detained before it is carried into the stomach. We have so far said in general terms that it is detained above the cardia. That the mass does not lie immediately above the cardia we could convince ourselves by direct ocular inspection, at least in rabbits. In these animals the part of the œsophagus situated below the diaphragm is easily accessible to full view, especially when, as in the above described observations, the stomach is lifted out of the abdomen. Then we could distinctly see that the swallowed mass never entered the part of the œsophagus below the diaphragm before the arrival of the peristaltic wave.

In dogs I have often introduced the finger through the cardia into the œsophagus, even above the diaphragm, and never could I feel the presence of the swallowed mass before the arrival of the peristalsis. I have also introduced short glass tubes into the œsophagus through the cardiac orifice, thus removing the obstacles possibly caused by the tonic contraction of the cardia; nevertheless the swallowed mass did not enter the stomach before the arrival of the peristalsis.

It could be urged, however, that the finger as well as the glass tube might, as foreign bodies, cause a local contraction of the œsophagus just above them and thus create an artificial bar to the further advance of the swallowed mass. I have therefore tried a method which permits direct inspection of the lower end of the œsophagus during rest and deglutition. A cut was made in the diaphragm near its anterior insertion, through which a speculum was introduced and pushed backward in the direction of the œsophagus. After permitting the lungs to collapse for a while I usually succeeded in adjusting the tube so as to have a good view of the œsophagus just above the diaphragm. The section of the œsophagus which could be seen

in this way was a little more than an inch in length. When the artificial respiration was discontinued and the dog was still in a state of apnœa the observation was easy and distinct. In all these observations the following phenomenon could constantly be demonstrated: The œsophagus was usually in a state of medium contraction and the beginning of the deglutition caused no change in it. A few seconds later the following series of incidents could be seen rapidly to take place: First, the œsophagus was drawn upwards, then strong bulging immediately followed, and right after this a strong transversal contraction swept downward, leaving the œsophagus for a while in a contracted state. During the period of bulging air bubbles could be recognized in the water or the milk. It was clear that in none of the deglutition acts was the swallowed food directly squirted down the œsophagus to as deep a point as the region under inspection, that is, about an inch above the diaphragm.

There now arose a quite embarrassing question. The fact that liquid food is projected down into the œsophagus with rapidity was learned by observations made only on human beings. Hamburger's deglutition murmur, heard alongside the spinal column, which indicates the rapid progress of the swallowed mass, has also been demonstrated up to the present only in human beings. Although Kronecker and myself have made numerous experiments on the œsophagus of dogs and rabbits, we have made them with a view of learning other facts and not for the purpose of ascertaining whether the swallowed mass progresses downward just as rapidly in these animals as we have proven to be the case in human beings. Now we find that in dogs and rabbits the swallowed mass is not squirted down directly into the stomach. We find, furthermore, that in dogs this mass does not reach even the level of the diaphragm. Perhaps, then, in animals the food is not projected down at all, but is carried down slowly by peristalsis.

Though our old tracings obtained from the œsophagus of dogs seemed to contain some material for an answer to this question, I preferred to obtain again direct ocular demonstration of the behavior of the upper part of the œsophagus during the act of deglutition.

For this purpose I have resected in dogs parts of the three upper ribs on the left side. When the artificial respiration was discontinued and the collapsed lung pushed aside by means of retractors, the entire upper part of the thoracic œsophagus was fully exposed to view. There it could be clearly seen that, when the dog was made to swallow by pouring some liquid into his mouth and pharynx, with each deglutition the liquid shot down through the exposed œsophagus long before any peristalsis reached there. The same thing occurred when the deglutition was caused by stimulation of the nerves, *i. e.*, when only air was thrown down in the œsophagus. This observation is in so far a new fact as it had not been and could not have been observed in the human being simply because it is impossible, at least for the majority of normal human beings, voluntarily to swallow air alone without any liquid. I shall here mention a fact which otherwise does not belong in this communication, but which brought out the fact of the swallowed mass being thrown down in the exposed œsophagus of the dog with great distinctness. In the anæsthetized animals it often occurs that the first act of deglutition takes place without being followed by peristalsis. We see in such an abortive deglutition how fluid or air is shot down in the œsophagus and remains there. If a few such abortive deglutitions followed one another in shorter or longer intervals, we saw the œsophagus swell up to quite a large size, looking like a "sausage," until a peristaltic wave set in and carried the entire mass downward all at once.

The appearance of such a considerable accumulation within the œsophagus gave rise to the further question whether it was not caused simply by a mechanical obstacle, *i. e.*, whether the left bronchus was not pressing upon the œsophagus in consequence of the horizontal position of the dog, thereby preventing the swallowed mass from entering the lower part of the œsophagus and reaching the stomach. Were this assumption true, we should still have before us the task to prove that when the animal is in a normal position the food is not directly squirted down into the stomach. The following observations, however, speak positively against such an assumption. In the first place, change of position, which could be easily accomplished, espec-

ially in rabbits, did not change our results; in no position of the animal did the swallowed fluid reach the stomach before the arrival of the peristaltic wave. Secondly, the accumulation of fluid or air within the œsophagus of the dog did not cease even when the left bronchus was lifted by means of a hook from its resting place upon the œsophagus. Furthermore, I have made the following more convincing observation. A piece of the left fifth rib was resected and a speculum was inserted in a manner which permitted the observation of the œsophagus at a point half-way between the diaphragm and the bifurcation of the trachea. I have then seen how sometimes immediately after the beginning of an act of deglutition a bulging appeared at this point of the œsophagus and remained there for some time until a peristaltic wave passed by and carried it downward. The detention of the swallowed mass at this point could not be due to any mechanical obstacle. Finally, after a close observation I have sometimes found that the mass thrown down, if it was small or projected with moderate force, did not reach even the point of the bifurcation.

It deserves to be mentioned that the direct ocular observation of the thoracic œsophagus conveyed to me the impression, first, that in a state of rest the lower part seems to be tonically more contracted than the upper part; and, secondly, that the upper part is distinctly more responsive to the changes of respiration than the lower part of the œsophagus. This latter fact is in conformity with our experience with the human œsophagus. As soon as the balloon was placed in the lowest segment the respiratory oscillations became less distinct.* These observations show that the lower portion of the œsophagus is in a pronounced state of tonic contraction, which may explain the resistance offered to the mass projected downward at the onset of deglutition.

My present observations justify, I believe, the following conclusions:

In animals, as well as in human beings, liquid food is not carried down the œsophagus by the slow progress of the peristaltic wave, but is thrown down rapidly into a deep part of this canal. This applies

* Compare Figs. 17 and 18 in the table of our article, Du Bois-Reymond's *Archiv*, 1883.

likewise to the swallowing of air alone, which is brought about in animals by stimulation of the superior laryngeal nerve.

As to the depth in the œsophagus reached by the immediately projected mass, this depends upon the quantity which is swallowed, upon the force with which it is thrown down, probably also upon the degree of tonicity of the lower portion of the œsophagus, and upon other variable circumstances. In no case did the swallowed liquid immediately reach even the level of the diaphragm, to say nothing of its shooting or oozing through the cardia into the stomach before the arrival of the peristalsis. It is, therefore, an experimentally proven fact that the swallowed mass is detained for some time within the lower part of the œsophagus, and that the position taken by Kronecker and myself concerning this question is correct.

That with each act of deglutition the swallowed mass should remain for a time within the lower portion of the œsophagus must, from a teleological point of view, appear strange indeed and might perhaps be brought into causal connection with the "spontaneous" development of such pathological conditions as dilatation of the œsophagus or the formation of an œsophageal diverticulum.

I shall append here a few brief remarks bearing upon the nature of the squeezing murmur. This murmur can be heard also in the dog, as has already been stated by Quincke.* It can be heard even at a distance when the stomach is well filled with air. This is best accomplished by introducing a tube into the stomach through the duodenum. By blowing up the stomach to different degrees it can be demonstrated that the loudness of the murmur depends largely upon the quantity of air present in the stomach, *i. e.*, the larger the quantity of air, the louder is the murmur, a fact which I pointed out long ago† and which was later confirmed by Quincke. This point is to be borne in mind in examining for this murmur, as it is hardly audible when the stomach contains only very little gas.

When the tube was in the stomach and the cardiac aperture con-

* Loc. cit.

† Meltzer, Zu den Schluckgeräuschen. *Berl. klin. Wochenschr.*, 1884, No. 30.

nected only with the air in the tube, the murmur was mostly very loud and sometimes reminded one of the explosive noise from a brass instrument. The character of the murmur depends apparently not only upon the size but also upon the shape of the vibrating column of air.

When I first described the squeezing murmur I stated that it had its explanation in the irregular vibrations of the tonically contracted cardia, the air within the stomach forming the sounding board. Quincke, however, compared the murmur with the bronchial râles. Without entering into a discussion upon the adequacy of such a comparison I wish here to say that while having the cardia under direct observation, its vibrations, during the formation of the murmur, could directly be seen.

Reprinted from the New York Medical Journal
for April 24, 1897.

[STUDIES FROM THE PHYSIOLOGICAL LABORATORY OF COLUMBIA UNIVERSITY, COLLEGE OF PHYSICIANS AND SURGEONS, VOL. I.]

THE EXPERIMENTS ON THE FARADIZATION OF THE STOMACH OF ANIMALS.

A REPLY TO DR. M. EINHORN'S CRITICISM, WITH A COMMUNICATION OF SOME NEW EXPERIMENTS.

By S. J. MELTZER, M. D.

I. In a paper read before the Association of American Physicians * I gave a condensed account of my experiments on the effects of faradization of the stomach and intestines of certain animals. It was my intention to make a strictly scientific statement of bare facts as I obtained them by physiological methods, without utilizing them for any practical purpose; and to avoid any misinterpretation, I expressly added that "my statements have reference only to the animals I have experimented with." My cautiousness, however, did not help me. Dr. M. Einhorn,† to my regret, has managed to discover that an "investigator has recently written against this therapeutic means (meaning the direct electrization of the stomach), basing his views entirely upon experiments made on animals." Desiring to defend the value of the direct electrization of the stomach as a therapeutic agent, Einhorn undertook, as he believes, a repetition of my experiments upon animals, and states that the results he ob-

* S. J. Meltzer. An Experimental Study of Direct and Indirect Faradization of the Stomach and Intestines. *New York Medical Journal*, June 15, 1895.

† Max Einhorn. *New York Medical Journal*, December 12, 1896.

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tained were in contrast to those I have stated, and were in perfect harmony with his view of the value of direct faradization of the stomach. In other words, he finds that those of my statements which are plain observations are simply not true, and those which are merely conclusions are false. Einhorn did not touch upon my experiments on the intestines—they do not seem to interest him; neither did he try to defend the percutaneous electrization, because this also does not interest him; nor did he say that even one single fact of my statements seemed to be somewhat true. In his experiments and his paper he had only one object in view, and that was to show that direct electrization was an efficient therapeutic agent, and that I, in my attack upon it, was totally wrong. Any reader who does not take the trouble of studying and comparing both papers carefully might think that Einhorn had simply repeated my experiments and found my statements to be untrue, and that the discussion was now reduced to the simple question of veracity between Dr. Einhorn and myself. I believe, however, I shall be able to reduce the importance of the experiments of Dr. Einhorn to their exact value without being compelled to touch upon the sensitive point of veracity. And as to this, I shall show later a plain way out of this dilemma.

II. It is an indispensable requirement for any experimenter who undertakes the task of verifying the statements of a predecessor, to observe at the repetition exactly the same conditions under which the original investigator professes to have observed his facts. Otherwise, the second man may bring out new results, but can not pretend to have reinvestigated the statements of the first experimenter. Let us now apply this simple desideratum to the experiments of Dr. Einhorn, who says he has shown that his results were in contrast to mine.

1. I have experimented on dogs, cats, and rabbits. I state that "the results obtained were verified in all the three kinds of animals; the greatest number of experiments, however, were made on dogs, which are best suited for our purpose. The stomach of the rabbit is

not a good object for studying the main phenomenon of our results." Frogs I have only used to see whether in this animal too the mucous membrane is less responsive than the serosa, a point which is not disputed by Einhorn; and even with regard to this point I say: "But this thick-walled stomach, with its small and slow contractions, was certainly not a desirable object for an extensive study of our phenomenon." For any of the other experiments frogs were never used. Now, Einhorn counts up seventeen experiments; twelve of them were made on frogs, two on rats, two on rabbits, and one on a dog. As I have not experimented on frogs (except as above stated) or rats, experiments on these animals do not concern me. There remain, therefore, only the experiments on the two rabbits and the one dog for a comparison with my results. And as I have stated already that the stomach of rabbits is not a good object for our study, especially when the animals had not previously fasted, which seems to have been the case in Einhorn's experiments, there practically remains only his single experiment upon the one dog upon which he bases his assertion that his experiments furnished results which were in contrast with those stated by me! We shall soon, however, see whether even this experiment has shown what Einhorn professes to have found. But even if it did, what does a fact signify when found only in a single experiment? I have expressly stated that "the results of my experiments represent only the rule, and do certainly not exclude the possibility of exceptions."

2. In my paper I have described in detail the method which I employed in the faradaic stimulation. Any one who would use the same Du Bois-Reymond's inductorium with a Grove cell, and have the secondary coil at the same distance from the primary, as in my experiment, would have exactly the same strength of current which I employed, and would thereby be in a position to ascertain whether certain reports of mine were correct or not. Dr. Einhorn does not mention at all what sort of apparatus and cells and what strength of current he employed: he says only that a faradaic current does this and that.

He speaks sometimes of a weak current, without giving us the means of judging what he understands by a weak current. We get, however, an idea of the strength of the faradaic current which Einhorn was employing when we read in his Experiments II and III that, when both electrodes are applied to the mucosa of the stomach, "the faradaic current produces contractions of the whole body." Such a current I never applied, and especially when I wished to study the local effects of a stimulus. Dr. Einhorn had no means by which he could compare the strength of his currents with that of those used by me, and he thus could not draw any conclusion as to the correctness of certain of my statements.

III. Let us now turn to the substance of Dr. Einhorn's assertions. In my experiments, so far as the stomach alone is concerned, there are four specific points which could come into consideration in our present discussion: 1. The fundus responds but little to faradaic stimulation. 2. A faradaic current which brings forth a maximal contraction when applied to the serosa produces no contraction when applied to the mucosa of the stomach. 3. When one electrode is applied to the serosa and the other to the mucosa, no contractions follow when the electrodes are separated by about two centimetres. 4. When one electrode is within the stomach and the other is on the skin near the stomach, no current brings forth a contraction of the stomach, etc. Einhorn does not mention the fourth point at all, though it is the main statement which could have some bearing upon the direct faradization of the stomach as a therapeutic measure. In taking up the three other points, Einhorn says that only the first and the third points "have direct reference to experiments on animals, the accuracy of which can only be ascertained by similar trials." The similar trials conducted by him led him to the assertion that his results were not in harmony with my statements. Leaving out for the present the analysis of Einhorn's peculiar handling of my statement contained in the second point, I shall now enter into a discussion of those two statements of mine which are directly denied by Einhorn.

1. When I made the observation that there was quite a striking difference between the contractility of the pyloric part of the stomach and that of the fundus, I thought it to be an entirely new fact. Now I know that a similar observation was made before me by von Ziemssen.* He also has found that the fundus of the stomach of dogs is nearly non-contractile when stimulated with the faradaic current. Some months after my communication Moritz † reported that during his studies upon the internal pressure of the human stomach, he had never observed any increase of the pressure taking place within the fundus; which means that the fundus never contracted during the observation. In the light of my own recent observations the fact of the diminished contractility seems to be rather an important one. I have studied it lately again and with greater detail, and will formulate my newer observations at a later point. I have already stated in my first paper that in the stomach of cats I could not establish such a difference of contractility between the fundus and the pyloric part. My statements, then, could surely not have been interpreted as being a generalization for all kinds of animals. As to the very small tubelike stomach of frogs, it did not even enter my mind to test whether there was a difference between the fundus and the pyloric portion. In dogs, however, the phenomenon is such a striking one that it is rather surprising to find that any one whose mind is already bent upon this point should not notice the outspoken difference in the contractility between the right and the left part of the stomach. The fact is, however, that in the single experiment XVII which Einhorn made on a dog, he describes his observations as follows: "The bipolar electrode is applied at the serosa of the fundus; a weak faradaic current produces a local contraction which is soon followed by a peristaltic contraction. . . . If the bipolar electrode is applied to the serosa of the pyloric portion of the stomach, the faradaic current produces *contractions of a more intense nature.*" That means that even in this

* v. Ziemssen. *Die Electricität in der Medizin*, 1887.

† Moritz. *Zeitschrift für Biologie*, vol. xxxii, p. 313.

single experiment Einhorn himself has indeed seen a distinct difference in the degree of the contraction between the pyloric part and some part of the fundus. Outside of this experiment on the dog, we are only concerned, as I have shown above, in his two experiments on rabbits. In one experiment (VII) it is not mentioned at all that the fundus was stimulated. In the other one, however, it is stated that the entire "gastric region," including the whole fundus, contracts when stimulated with the faradaic current. Whether there was any difference in the degree of the contraction or not is not expressly noted. But even if there was no difference at all between pyloric part and the fundus, what weight can this single experiment have? and an experiment on a filled stomach of a non-fasting rabbit, the contractions of which are at all times quite indistinct! However, above all, it is my impression that Einhorn never had before him the entire fundus of any of the larger animals he experimented upon. In order to obtain a full view of the left part of the stomach it is necessary to have this part, together with the spleen, lifted out from the abdominal cavity. To keep it in view after lifting it up, I have usually had it supported with some instruments or sewed to the abdominal wall, which latter is the more practical method. Einhorn, however, states only: Abdomen opened, or stomach exposed, or (on one occasion) stomach pushed forward—which does not seem to mean that he had the spleen and the left end of the stomach entirely out of the abdominal cavity. What Einhorn has seen and stimulated might, then, have been only the middle and a small portion of the left side of the stomach.

But leaving any explanation aside, the bare facts in the three experiments of Einhorn, the only ones which might concern us, are the following: In the single experiment on the dog there was indeed a distinct difference in the degree of contraction between the pyloric part and the fundus; in one rabbit the bipolar stimulation of the serosa of the fundus was not attempted at all (it is at least not mentioned in the experiment), and in one non-fasting rabbit the bipolar stimulation of the fundus

brought on contractions. It is, then, on the basis of this single experiment on the rabbit, with its, in many respects, doubtful value, that Einhorn bases his assertion that the results of his experiments were in contrast to those of mine. And on the basis of these experiments he believes himself justified in stating, in a general and a positive way, " that in rabbits, rats, dogs, and frogs," the bipolar (faradaic) electrization of any part of the gastric serosa, including the fundus, produces contractions, etc. Rabbits and dogs—with at the utmost one rabbit and one dog at his disposal!

2. The second point concerning which Einhorn professes to have found results opposite to those I have reported refers to my statement that when one electrode is applied to the mucosa and the other to the serosa, the faradization does not call forth a contraction. I wish to state beforehand that I do not lay too much stress upon this point, because it is neither of practical nor of great physiological importance. It is not of practical importance, because nobody has electrized a stomach for therapeutic purposes by applying one electrode directly on the serosa of the stomach; and it has no special physiological importance, as it is to a great extent contained already in the fact of the diminished responsiveness of the mucosa. We must also recur to some particulars of the later fact in order to understand the point in question. I have stated, in my paper, that a " strong current " (for instance, such current as is obtained when the secondary coil is at a distance of a hundred and twenty to a hundred and thirty millimetres from the primary), which produces a maximal contraction when both electrodes are applied to the serosa, does not have any effect upon the muscularis when both electrodes are applied to the mucosa. " Very strong " currents, however (like those of a distance of forty or fifty millimetres, and sometimes even of eighty or ninety millimetres), do often produce a contraction even when applied to the mucosa. I have then further stated briefly that even when one electrode is applied to the mucosa and the other to the serosa, a strong current does not produce a contraction

unless both electrodes are within two centimetres' distance from each other. I did not dwell further upon this point; but it must be clear enough to every one that such a " very strong " current, which is sufficient to bring on a contraction even by having both electrodes on the mucosa, will certainly produce a contraction when one electrode is placed on the mucosa and the other on the serosa. Now, Einhorn, who professes to have found that the stomach contracts when stimulated by one electrode on the mucosa and the other on the serosa, has used a faradaic current of unknown strength. We are thus unable to determine whether his observations were in harmony with mine or not; the fact mentioned in his protocols, that a bipolar stimulation of the mucosa could produce contractions of the entire body of the animal, shows that Einhorn has stimulated with currents far stronger than even those which I term " very strong." By the way, in the small stomach of frogs, the animals which were mostly experimented upon by Einhorn, it is hardly possible to have the distance between the inner and the outer electrode greater than two centimetres—a distance within which I have stated that a contraction takes place even in dogs. Furthermore, these experiments, one electrode on the mucosa and the other on the serosa, I have made nearly exclusively on fasting dogs, the inner electrode being introduced into the stomach through the mouth, as in these experiments the stomach was never opened in order to exclude a possible circuit: mucosa + cut + serosa. In Einhorn's experiments, at least on the two rats, one rabbit, and the one dog, the inner electrode was introduced through an opening in the stomach. In the single experiment on the dog, the only one which could at least in some sense be compared with my experiments, Einhorn writes as follows: " The stomach is opened; one electrode is held at the gastric mucosa, the other at the serosa (fundus); a weak faradaic current produces a light peristaltic contraction." He, then, has not seen a local constriction, but a light peristaltic contraction. What I am speaking of in my paper is not a peristaltic but the local contraction, and I have stated express-

ly "that in studying the effects of a stimulation it is necessary to be aware of the accidentally passing by of a peristaltic movement, which might be mistaken for a local contraction."

Einhorn's contention, then, that when stimulating with one electrode on the mucosa and the other on the serosa he obtained results opposite to those reported by me, is utterly unfounded. He worked under uncontrollable and different conditions from those which were observed in my experiments, and has seen and been satisfied with other phenomena than those which I have described.

IV. A rather strange treatment was accorded by Dr. Einhorn to one other point in my paper: it is the oftenmentioned fact that, when both electrodes were applied to the mucosa, even a strong current did not produce a contraction. Throughout my paper I consider this phenomenon to be the most striking observation in my experiments. In the mouth, pharynx, and œsophagus, even over the unstriated muscle fibres, a stimulation of the mucous membrane produces a contraction of the muscles beneath it without any difficulty. Even in the intestines the obstacle which the mucous membrane forms to the penetration of the current is small in comparison to that observed in the stomach. On the mucous membrane of the stomach, however, even on that part which spreads over the thick muscular wall of the pylorus, strong currents do not reach the muscular coat at all. This fact, so far as I know, was entirely new. In the entire paper I have not attempted to give any explanation of this phenomenon. I have spoken a few times of the "resistance" the mucosa offers to the penetration of the current, simply as a matter of convenience, to use a single word instead of a whole sentence; but have expressly added: "What the resistance means, what is its nature and extent, I should not attempt to answer for the present; it is reserved for a further study." Now Einhorn does not mention with one single word that I have observed such a new fact. He notes this fact in his experiments, he states it (by the way, in a wrong and very dilute form) in his *résumé*, but fails to state that this might be a con-

firmation of at least one of the facts which Meltzer professed to have observed. But what Einhorn does say in this respect is this: After counting up the two points where Meltzer simply misstated facts, Einhorn says: "3. The resistance of the gastric mucosa, according to Meltzer, is different from that of all other mucous membranes, being here very great"; this "third point is merely theoretically constructed, and, it appears to me, on a false basis." So, then, where Dr. Einhorn could not find fault with the fact itself, he omits to mention that I was the first to observe and state it, but instead he discovers that I have put up a theory which is, as it appears to him, false. Does Dr. Einhorn believe that if I had had a theory to put forward, I would not state it directly, but leave it to be implicitly understood by using a single word? And should not my express statement that I did not for the present wish to give any interpretation to the word resistance have protected me against the imputation of offering any theory? However, let us see why Einhorn finds my theory to be false. He says that Meltzer assumes "that the current *can not* penetrate the mucosa and reach the muscular layer." "It appears to me [Einhorn], however, much more probable and natural to presume that the gastric mucous membrane is a very good current conductor. But just for this reason the current will run merely to this membrane and not reach the muscularis. The electric current always takes the shortest path, the one which offers least resistance." Well, if the path *along the surface of the* mucous membrane offers the "least resistance," then the path *in the direction through the thickness of the membrane* will offer a "greater resistance"; that is all that I meant when speaking of the greater resistance of the mucosa. Where, then, is the contradiction between Einhorn's true and my false theory? It seems to me that either I do not understand Einhorn's point, or else Einhorn has neglected to analyze clearly the points under consideration. To repeat again, I simply wish to say that in the penetration in the direction of the thickness of the membrane toward the muscularis the current meets in the stomach with

an unusual obstacle, a resistance. Whether this occurs on account of the exceptionally good conductivity of the surface of the mucous membrane of the stomach, while the conductivity in the direction of the thickness is the same in this membrane as it is in any other mucous membrane; or whether the conductivity of the surface of the mucosa of the stomach is the same as in any other mucous membranes, but the conductivity in the direction of the thickness is here abnormally less on account of some layers, glands, etc.; or whether the acid reaction has anything to do with the increased resistance; or whether this is on account of a peculiar arrangement of the submucosa, etc.—I do not wish at present to decide between or even to discuss all the possibilities. Although I already have some facts which might throw some light in a certain direction, they are not numerous and certain enough to decide this problem with a scientific probability; and I am not willing to follow the example of Dr. Einhorn in making general and positive statements after having made a hasty experiment on a single dog, or a single rabbit, or a single Morris S. By the way, I shall abstain from discussing the value of Einhorn's experiment with Morris S., as it does not purport to affect any of my statements. I have no desire to write here any other criticism than such as is necessary to refute Einhorn's attack upon my statements.

V. The avowed purpose of Dr. Einhorn's experiments and paper was to prove the efficacy of direct electrization as a therapeutic means, against which, according to Einhorn, I have written. Let us now examine exactly how far Einhorn has succeeded in his purpose. Let us even assume that his experiments have shown all that he wanted to show. He has, then, shown that my statement about the fundus is not true, and that my theory of the increased resistance of the mucous membrane is false. Well, these points have nothing to do with electrization as a therapeutic agent. But Einhorn has also shown my statement with regard to electrization with one electrode on the mucosa and the other on the serosa to be untrue. As there is no other refutation of any of my state-

ments, it is probably on the strength of this latter contention that Einhorn draws the conclusion: "3. If one electrode is within the stomach, and the other applied to some other part of the body (leg, arm) which is not too far away from the stomach, a faradaic current of medium strength, lasting twenty to thirty seconds, produces peristaltic contractions of the stomach in addition to the part at which the outside electrode is held." Einhorn says here it produces peristaltic contractions of the stomach. In all the seventeen of Einhorn's experiments there is only one where it is mentioned that if one electrode is on the mucosa and the other on the serosa, the faradaic current produces a light peristaltic contraction (Experiment XVII), and that was in the often-mentioned single experiment on a dog; and, judging by the way the description reads, it would seem that there was altogether only one single stimulation. Here, again, Einhorn seems to generalize from a single experiment, or perhaps from a single stimulation! But leaving all these extremely weak points aside, Einhorn could not seriously mean to say that because stimulation with one electrode on the mucosa and the other on the serosa produces a contraction, this must also be true when the other electrode is placed on the skin of the body instead of on the serosa of the stomach? Why, altogether, has Einhorn avoided mentioning that point of my experiment which has a direct bearing on the question at issue? I have stated that when one electrode is on the stomach and the other on the skin near the stomach, this organ remains perfectly motionless, and I have shown even more, that under these circumstances there is not a current on the serosa of the stomach sufficient to stimulate even the sciatic nerve. Now, if any of my statements can be interpreted as being against faradization as a therapeutic measure, it is surely the one I have just recorded. Why, then, has Einhorn not mentioned it, and why did he not repeat just these experiments, if he intended to refute the main damaging contention of mine?

But there is still a greater surprise in store. Though

Einhorn has avoided mentioning that I have made such experiments, and though he does not say that he made such experiments, he made them nevertheless, but with what a result! Here they are: " Experiment I.—Frog: One electrode is introduced through the mouth into the stomach . . . ; if the outer electrode is placed on any part of the body (leg or abdominal wall), then the faradaic current produces contractions of the body, while there is apparently nothing visible with regard to the stomach." " Experiment XV.—Frog: Abdomen opened; one rubber electrode within the stomach. . . . If the stomach is covered with the abdominal wall, and the other electrode applied at the skin, the faradaic current produces either no contraction whatever of the stomach, or a slight one; while there are always contractions of the abdominal muscles." In these two experiments, Einhorn has seen distinctly that, when one electrode is within the stomach and the other on the abdominal wall, the faradaic current does not bring on a contraction of the stomach, and this even in such short distances as exist in frogs! Nevertheless, Einhorn calmly draws his above-quoted exactly opposite conclusion: " 3. If one electrode is within the stomach and the other applied to some part of the body . . . a faradaic current of medium strength . . . produces peristaltic contractions of the stomach in addition to the contractions of the part at which the outside electrode is held " ! Further comment is surely not required.

VI. Dr. Einhorn was carried away in his, to say the least, very hasty work by his zeal to defend direct faradization as a therapeutic measure. But what made him assume that I had attacked it? I only stated that direct and cutaneous faradization did not produce a contraction of the stomach in the animals I had experimented with. I did not say that the same conditions must prevail in human beings, and I did not deny that faradization could produce other useful effects besides contractions of the stomach. And why was Dr. Einhorn more annoyed by my statements than by the statements of those who went

even further than I did. Moritz,* for instance, has found that direct faradization, the inner electrode being in the fundus or in the pyloric part, does not cause any contraction of the human stomach, as judged by the change in the "internal pressure" of the stomach. And Goldschmidt † goes so far as to state that neither the faradaic nor the galvanic current has either a motor or a secretory effect; the latter point in direct contradiction to the statement of Einhorn, to whose figures Goldschmidt does not attach much importance.

This Goldschmidt states in the "physiological part" of his article; in the "clinical part" he simply reports a number of stomach cases which were improved by treatment with electricity, and confesses that he is unable to offer any explanation of the therapeutic results. Why was Dr. Einhorn not charitable enough to assume that I might hold a similar position to that of Goldschmidt? He would have saved himself and me the trouble and the annoyance of a perfectly superfluous controversy.

VII. Dr. Einhorn, in his article, has simply stated that the results which he found in his experiments were in contrast to those stated by me, leaving to the reader the choice between my ability or my veracity, as to which should be held responsible for my statements. Were I myself to have the selection, I should decidedly prefer to have my ability doubted than my veracity. Applying the same rule to Dr. Einhorn, I have so far avoided supporting my statements by reference to competent men of science who witnessed my experiments, and who can testify in behalf of the truthfulness of my statements, thus leaving Dr. Einhorn in a similar dilemma, or rather in a worse one than he chose to put me in. However, there will yet remain some readers, especially those whose clear judgment is biased by the same motives which misled Einhorn, who will not be convinced by my arguments. For the benefit of such readers, and in justice

* *Loc. cit.*

† *Deutsch. Archiv für klinische Medizin*, vol. lvi, p. 295.

to myself, I wish to make the following personal statements:

My work was done in the physiological laboratory of the College of Physicians and Surgeons in the winter of 1894–'95. I was then working on the problem of the effect of the vagus upon the contractions of the stomach. In the course of this research I came to stimulate the stomach directly with the faradaic current, and then made the surprising observations under discussion. I worked out these observations systematically on many animals. I had no practical object whatsoever in view while pursuing this study, and certainly did not think of interfering with any one's therapeutic preferences. I wish to say in my own behalf that, though being myself a practitioner and intensely interested in the proper advancement of practical medicine, I make it a point never to permit any practical considerations to enter into the selection and pursuit of a purely scientific, a physiological, or a biological problem. I have two reasons for it: one is a personal one—it is my inclination; the other is founded in my firm belief that one arrives, in the solution of a problem, much nearer the truth the less his judgment is biased by practical motives, and that an unbiased truth will be of more practical service than one discovered to order.

I have often called upon my friends in the laboratory to witness the phenomena, to confirm or to contradict, and to discuss their meaning. In the course of this winter, too, I have again taken up the same line of experiments, which have often been witnessed by the members of the laboratory staff. I am permitted to refer to Professor F. S. Lee and Dr. R. H. Cunningham, who have often seen my experiments and can confirm my statements of experimental fact. Furthermore, I demonstrated the main facts under discussion to the members of the American Physiological Society, in the physiological laboratory of the Harvard Medical School, Boston, on December 29, 1896 (see *Science;* January 29, 1897).

Possibly the question will not yet be settled for Dr. Einhorn, and he will be inclined to continue the dis-

cussion much longer. In order not to waste his and my time, I make the following proposition: I will leave it to Dr. Einhorn to select a few men of science who are capable of passing judgment upon the question under discussion, and I am ready to experiment in their presence. If I fail to sustain my statements, they can say so; if I succeed, they shall state so. This will settle the scientific dispute. Unless Dr. Einhorn complies with this proposition I shall consider my discussion with him on this issue as closed.

VIII. I have above mentioned that I have lately again taken up the study of the contractility of the stomach. In close connection with the foregoing I wish to append here briefly a few of the results I have so far obtained, and of which I have already given a short account at the above-mentioned annual meeting of the American Physiological Society.

In all the dogs I have so far experimented with, a stimulation of the peripheral end of the pneumogastric nerves caused a distinct contraction of the stomach. In one dog this effect was obtained only by the stimulation of the left, and in another only from the right nerve. Usually the effect can be obtained from both nerves, though there are nearly always some differences. For instance, a stronger current is sometimes required for one nerve than for the other in order to produce an effect; or the effect is stronger from one than from the other. The weakest effective current shows sometimes during stimulation a very moderate peristaltic movement of the stomach, sometimes the effect is not seen until the stimulation is discontinued—after-effect. Strong stimulation does not cause a peristalsis, but a simultaneous contraction of an entire part of the stomach. The contraction is the stronger the stronger the current is and the longer the stimulation lasts. However, the contraction seems always to attain its maximum only after the cessation of the stimulation. This fact is highly interesting, but has not yet been studied well enough to dwell upon it here any longer.

The fact to which I wish especially to direct attention is this:

No matter whether the right vagus or the left, or both vagi were stimulated, the contraction was always confined to the right part of the stomach. The stronger the stimulation and the longer it lasted the larger was the part which became involved in the contraction; but always quite a large part of the left side of the stomach remained unaffected by the contraction, except that it received the gas from the contracted part. We should not dwell here upon further particulars of this phenomenon.

While having the stomach of a fasting or fed animal under observation I have often enough seen spontaneous peristaltic waves passing over the stomach. But since my attention was directed to the difference between the right and the left part of the stomach I have never seen a distinct peristaltic movement passing over the outer end of the left side of the stomach. Whether a movement started in the fundus and traveled toward the pylorus, or started in the pylorus and traveled toward the left, the contraction was always stronger at the pylorus, and gradually lost its intensity (and duration) while traveling toward the left, until it reached about the outer third, when the contraction ceased to be distinct and easily recognizable.

The very same description fits exactly to the very lively peristaltic movements which sometimes take place when asphyxia sets in. The outer end of the left part of the stomach does not seem to take part in the lively commotion.

I have often caused purposely, as well as involuntarily, the starting of a peristaltic wave by a mechanical stimulus. It was always confined to the bulk of the right part. I never could cause the starting of a peristaltic motion by stimulating the outer end of the left part of the stomach. The same applies to thermal and chemical stimuli. With electrical stimulation (faradaic) I have, so far, rarely succeeded in causing a plain peristaltic move-

ment. When it did happen, it was caused by only a very light stimulus, and was confined to the outer end of the pyloric part. However, nearly every strong local contraction caused by an adequate faradaic stimulus winds up with a moderate peristaltic wave.

I have studied again, and in greater detail, the difference in the behavior between the right and the left part of the stomach, with regard to the local effect of direct stimulation with the faradaic current. The following short statement is derived from my present experiences. We might consider the contractility of the stomach, with regard to faradaic stimulation, as having a negative and a positive pole. The outer end of the fundus represents the negative, and the pylorus the positive pole. There is generally a gradual transition between the two poles. In all the animals (dogs) which I have so far examined there was at the outer end of the fundus an area where no distinct contraction could be produced by any current, no matter how strong. In two cases there was a slight shriveling confined to the part next to the electrodes and to the uppermost layer of the muscularis. On moving the electrodes more toward the right end of the stomach, the local contraction became more and more distinct, and it reached its maximum at the pylorus. The place where the first distinct contraction can be produced rests largely upon the strength of the currents; the stronger the current the farther to the left is the first distinct contraction obtainable. A current of medium strength (about a hundred and thirty millimetres' distance of the secondary from the primary coil on a Du Bois-Reymond inductorium) produces distinct contractions only in the pyloric part.

All these experiments are full of important practical consequences, which, however, I do not intend to draw attention to for the present. Availing myself of this opportunity, I wish to express my gratitude to Professor John G. Curtis, the director of the physiological laboratory of the College of Physicians and Surgeons, for the courtesy shown me by affording to me, now for many years, the

rare opportunity of pursuing some original researches in this progressively equipped laboratory. I wish also to thank my friend Professor F. S. Lee for the constant interest he has taken in the various researches I have there pursued, and for the many valuable suggestions on and discussion of the problems involved in these researches.

Studies from the Departement of Physiology of Columbia University
at the College of Physicians and Surgeons, New-York, vol I.

Einige allgemeine Eigenschaften

des

Herzmuskels vom amerikanischen Hummer

(Homarus Americanus).

Von

Reid Hunt, Ph. D., **A. Bookman**, A. B.,

und

M. J. Tierney, A. M.

Reprinted from the „Centralblatt für Physiologie" Bd. XI, p. 274, 1897.

LEIPZIG UND WIEN.
FRANZ DEUTICKE
1897.

Einige allgemeine Eigenschaften des Herzmuskels vom amerikanischen Hummer (Homarus Americanus).*)

Von **Reid Hunt**, Ph. D., **A. Bookman**, A. B., und **M. J. Tierney**, A. M.

Für die hier angeführten Experimente wurde das Herz aus dem Körper herausgenommen, und in einer feuchten Kammer nach der Art der gewöhnlichen Muskelnervenpräparate aufgehängt. Die Temperatur war, wo es nicht anderweitig bemerkt ist, diejenige des Zimmers, 17° C.

Die Contractionen wurden mittelst eines sehr empfindlichen Hebels auf der Trommel eines Baltzar'schen Kymographions verzeichnet.

Nach der Entfernung aus dem Körper fuhr das Herz für einige Zeit fort spontan zu schlagen, kam aber nach einem bald längeren, bald kürzeren Zeitabschnitte zur Ruhe. Es blieb jedoch erregbar und antwortete auf faradischen Reiz für einige Zeit, nachdem es bereits spontan zu schlagen aufgehört hatte.

Latenzstadium der Contraction.

Das Latenzstadium der Contraction vom Herzen des Hummers (bestimmt mittelst der gewöhnlichen Methode von Helmholtz) ist im Vergleiche mit demjenigen des Froschherzens sehr kurz.

Die Länge desselben wechselt sehr bedeutend, je nach dem Zustande des Herzens, aber beträgt gewöhnlich $^1/_{50}$ einer Secunde; es kann jedoch hin und wieder nur $^1/_{100}$ Secunde, manchmal aber auch $^1/_{25}$ Secunde betragen.

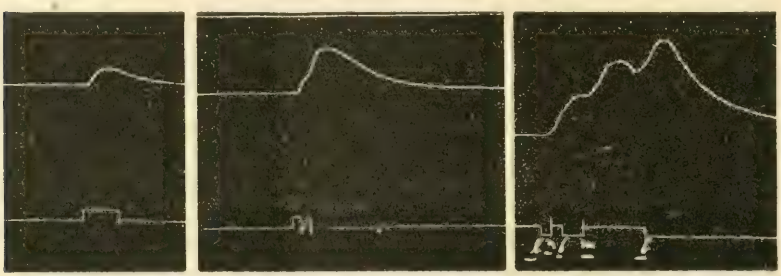
Refractäres Stadium.

Das für das Herz der Vertebraten so charakteristische refractäre Stadium, d. h. ein Stadium der Contraction des Herzens, während

*) Die hier angeführten Experimente wurden einem von uns (R. H.) durch seinen früheren Lehrer, Prof. W. H. Howell, welcher beobachtet hatte, dass im Krabbenherzen durch elektrischen Reiz Tetanus hervorgerufen wurde, vorgeschlagen.

welcher dasselbe auf Reize nicht antwortet, ist im Herzen des Hummers bei Zimmertemperatur nicht vorhanden. (Wir haben das Latenzstadium diesbezüglich nicht näher studirt.)

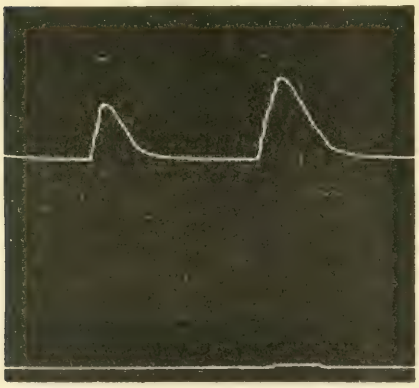
Das Herz antwortet direct, und augenscheinlich mit unverminderter Kraft auf elektrische Reize während aller Phasen der Con-



A *B* *C*

Fig. 1. *A*. Einzelne Contraction nach einem Schliessungsinductionsschlage. *B*. Summation der einzelnen Contractionen, resultirend von zwei Schliessungsinductionsschläge. *C*. Summation der Contractionen, hervorgerufen durch fünf Reize [Schliessungs- *(m)* und Oeffnungs- *(b)* Inductionsschläge].

traction, sowohl während der Systole (Fig. 1 und 2 *B*) als auch während der Diastole (Fig. 3). Die Erscheinung findet auch statt,



A *B*

Fig. 2. *A*. Eine spontane Contraction. *B*. Es wurde ein einzelner schwacher Inductionsschlag während der Systole einer spontanen Contraction eingeschaltet.

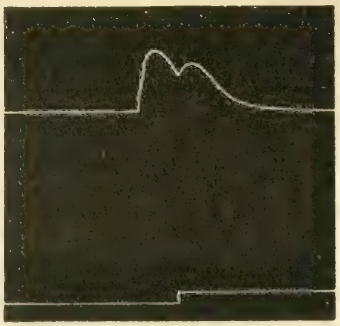


Fig 3. Resultat der Einschaltung eines minimalen Inductionsschlages während der Diastole einer spontanen Contraction.

wenn man sehr schwache Reize anwendet: die Contraction, während welcher gereizt wird, mag eine spontane oder eine durch elektrischen Reiz hervorgerufen sein.

Wenn jedoch das Herz einer niedrigen Temperatur (5° C.) ausgesetzt wird, so nimmt seine Reizbarkeit ab, und zwar mehr während

der Systole als während der Diastole; das Herz antwortet dann nicht mehr auf einzelne, sondern nur auf zwei oder mehr schnell aufeinander folgende Inductionsschläge.

Summation von Contractionen und Tetanus.

Wie man erwarten sollte, da während der Contraction kein refractäres Stadium besteht, kann man im Herzen des Hummers Summation von Contractionen (Fig. 1, 2 und 4) und wirklichen Tetanus (Fig. 5 und 6) sehr leicht erzielen. Die Contraction, welche durch

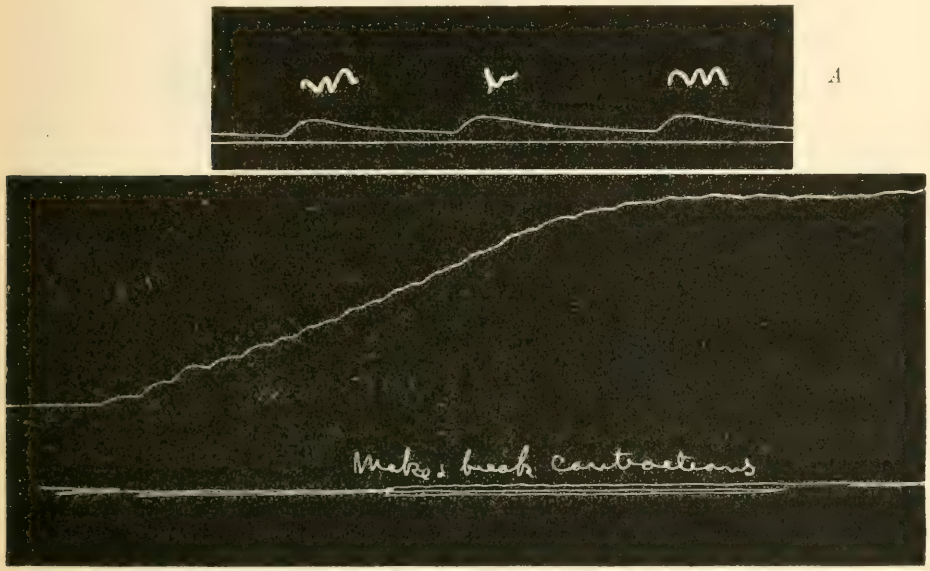


Fig. 4. *A*. Contractionen, hervorgerufen durch einzelne Schliessungs- *(m)* und Oeffnungs- *(b)* Inductionsschläge. *B*. Summation der Contractionen, hervorgerufen durch rasch aufeinander folgende Oeffnungs- und Schliessungsinductionsschläge.

tetanischen Reiz des Herzens hervorgerufen wird, ist vielmals stärker als eine einzelne (maximale) Contraction (Fig. 4 und 5).

In dieser Hinsicht unterscheidet sich der Tetanus des Hummerherzens in prägnanter Weise von dem sogenannten Tetanus, wie er manchmal für das Froschherz beschrieben wurde.

Vollkommener Tetanus wird durch tetanischen Reiz ebenso leicht bei niedriger Temperatur ($3^1/_2{}^0$ C.) erzielt als bei höherer, trotzdem das Herz, besonders während der Systole, unter diesen Verhältnissen weniger empfindlich gegen einzelne Inductionsschläge ist.

Die Anzahl der Reize pro Secunde, welche nöthig ist, um vollkommenen Tetanus zu verursachen, wechselt je nach dem Zustande des Herzens; bei einem frisch präparirten kräftigen Herzen waren sechs

oder mehr Reize pro Secunde erforderlich; bei einem schwachen, erschöpften Herzen genügten zwei Reize in 3 Secunden. Reize, welche zu schwach waren, um einen merkbaren Einfluss auf das Herz auszu-

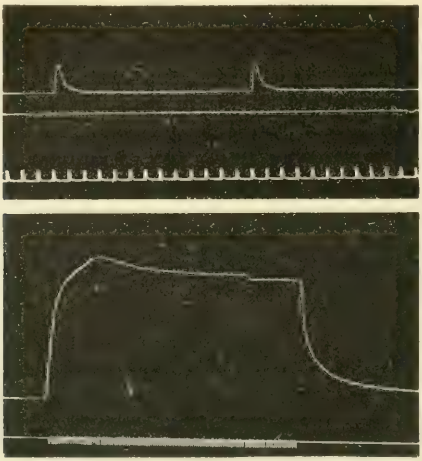


Fig. 5. *A*. Contractionen, hervorgerufen durch einzelne (maximale) Inductionsschläge. *B*. Vollkommener Tetanus durch rasch wiederholte Inductionsschläge. Zeit in Secunden. Die untere Linie in *B* zeigt die Anzahl der angewendeten Reize.

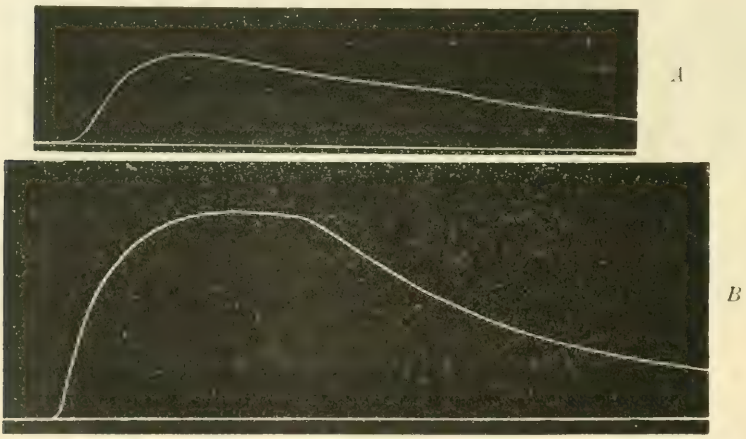


Fig. 6. *A*. Vollkommener Tetanus durch die Anwendung eines tetanisirenden Inductionsstromes; Rollenabstand 10 Centimeter. Einzelne Inductionsschläge von dieser Stärke waren ohne sichtbaren Effect. *B*. Vollkommener Tetanus; Rollenabstand 4 Centimeter.

üben, wenn sie einzeln angewendet wurden, bewirkten vollständigen Tetanus bei rascher Aufeinanderfolge (Fig. 6 A).

Das „Alles oder Nichts"-Gesetz.

Dieses Gesetz ist auf das Hummerherz nicht anwendbar; es ist nämlich nicht jede Contraction eine maximale, wie im Froschherzen, sondern die Höhe der Contractionen steigt (bis auf ein Maximum) mit der zunehmenden Stärke der Reize (Fig. 7). Dies findet sowohl während tetanischen Reizes (Fig. 6) als auch bei der Anwendung einzelner Inductionsschläge statt.

Wir sehen also, dass der Herzmuskel des Hummers, obgleich er die Fähigkeit der automatischen und rhythmischen Contraction in hohem Maasse besitzt, gewisse hervorragende Eigenthümlichkeiten des

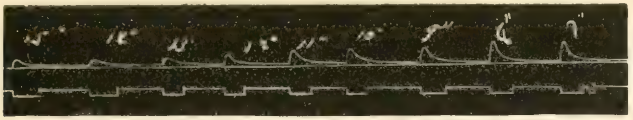


Fig. 7. Zunahme der Höhe der Contractionen mit wachsender Stromstärke (einzelne Inductionsschläge). Die Figuren zeigen die Stellung der secundären Rolle an. (Aller Wahrscheinlichkeit nach ist dies kein Treppenphänomen, da mehrfache Reizung mit Strömen derselben Stärke keine Zunahme in der Höhe der Contractionen bewirkten.)

Herzmuskels der Vertebraten (Unfähigkeit in wirklichen Tetanus zu verfallen), entweder gar nicht, oder nur in sehr geringem Maasse (Verlust der Reizbarkeit während der Contraction) aufweist.

Der Herzmuskel des Hummers nimmt also thatsächlich physiologisch eine Mittelstellung zwischen dem gewöhnlichen Skeletmuskel und dem Herzmuskel der Wirbelthiere ein; wie der Skeletmuskel wird er mit Leichtigkeit in Tetanus versetzt, und ist während aller Stadien der Contraction erregbar (ausgenommen bei niedrigen Temperaturen), und wie der gewöhnliche Herzmuskel besitzt er in hohem Masse die Fähigkeit der automatischen und rhythmischen Contraction.

Es ist daher anzunehmen, dass die rhythmische Bewegung des Herzmuskels nicht nothwendigerweise in so enger Beziehung zu den anderen Eigenthümlichkeiten dieses Muskels steht, als oft angenommen wird.

K. u. k. Hofbuchdruckerei Carl Fromme in Wien.

Studies from the Department of Physiology of Columbia University, at the College of Physicians and Surgeons, New York.

Reprinted from the American Journal of Physiology, Vol. I, 1898.

ON THE NATURE OF THE CARDIOPNEUMATIC MOVEMENTS.

By S. J. MELTZER.

[*From the Department of Physiology of Columbia University, at the College of Physicians and Surgeons, New York.*]

FOR more than thirty years it has been known that the air in the respiratory tract shows slight periodical oscillations, synchronous in rhythm and time with the cardiac beats, — the cardiopneumatic movements, as they have been called since Landois first gave them the name.

C. Voit[1] observed these movements while breathing through a Müller's valve. During a respiratory intermission in which the glottis remained open and the nose closed, regular oscillations were noticed consisting of tiny inspirations and expirations. Voit found the inspiratory motion synchronous with the systole, and the expiratory with the diastole of the heart. He explained the phenomenon by the assumption that each systole — diminishing the volume of the heart — causes a lowering of pressure within the thoracic cavity, and thereby an aspiration of air by the lungs, — an inspiration; while the diastole increases the pressure, and causes an expiration.

Two years later Terné van der Heul,[2] under the direction of Donders, attempted to get tracings of these movements as they are obtainable from the nose, and was surprised to find that, in his case, the inspiration coincided with the diastole and the expiration with the systole, the tracing presenting a regular sphygmogram. It is probable, however, that in van der Heul's case the glottis was closed while the tracings were taken, these therefore being in fact nothing but sphygmograms, *i. e.*, the variation in the volume of blood within the closed cavity of the nose. Many persons, as Mosso has shown, are indeed unable to keep the glottis open while they stop breathing. The writer of this article can witness to that fact. In the few attempts which he has made to obtain cardiopneumograms from the nose the result has been invariably a sphygmogram.

[1] Voit: Zeitschrift für Biologie, 1865, i, p. 390. The phenomenon had already been described before Voit by Buisson, Gaz. med. de Paris, 1861, p. 320.

[2] Terné van der Heul: Nederlandsch Archief voor Genees- en Natuur-Kunde, 1867.

Ceradini[1] studied the movements at first by means of a manometer connected with the nose or mouth, and containing smoke or colored liquid; he confirmed the statement of Voit, and also adopted his explanation of the phenomenon. In a later study,[2] however, Ceradini modified his first interpretation. He came to the conclusion that the systolic condition of the heart could not change the pressure within the thoracic cavity as long as the blood put out from the left ventricle is still within the cavity. Ceradini, therefore, now assumed that the oscillations did not originate from the change in the volume of the heart, but from the change in the volume of blood present in the thoracic cavity; the inspiration being due to the outflow from the cavity of the chest, and the expiration due to the inflow of blood into the cavity. Ceradini also obtained tracings of these movements by means of an instrument which he called "Hæmothorakographion,"[3] but never published them.

In 1876 Landois[4] published an elaborate monograph on these oscillations, which he termed, as stated above, cardiopneumatic movements. He studied the movements with the aid of the manometric flame, and, also, by means of his cardiopneumograph, obtained tracings of them from the nose and mouth of men and from the trachea of curarized dogs. The skeleton of his tracings shows a sudden steep inspiratory, and a gradual, slanting expiratory undulation, which Landois, adopting Ceradini's later view, explains by the sudden arterial output of blood from, and the gradual venous flow of blood into, the thorax. Besides these main movements, Landois noticed on his tracings little secondary notches and peaks which he attempted to explain by certain subsidiary but constant causes. The rebound of the arterial blood causes a tiny peak on the expiratory line. Landois insists that each inspiratory movement is preceded by a small sharp expiratory motion, which he explains by an assumption that I shall not discuss here. Mosso,[5] on the other hand, who accepts the views of Ceradini and Landois with regard to the chief cause of these movements, claims that no short respiratory upstroke precedes the inspiratory movement, and that, in his opinion, the beginning of this latter

[1] CERADINI: Heidelberger Jahrbücher der Literatur, 1869, p. 912.

[2] *Ibid.:* Annali universali di medicina, 1870, p. 587.

[3] This instrument, as well as the cardiopneumograph of Landois, is practically nothing more than a Marey's tambour.

[4] LANDOIS: Graphische Untersuchungen über den Herzschlag. Berlin, 1876.

[5] MOSSO: Die Diagnostik des Pulses, 1879.

movement is caused by the widening of the chest due to the heart impulse.

Finally, Martius, who wrote a very elaborate article on the "cardiopneumatic movements in the œsophagus," should also be mentioned, but I shall not discuss his article here. I wish only to say that Martius, in his very elaborate analysis of his tracings, also adopts the view that the flow of blood into and out of the thorax is the chief cause of the cardiopneumatic undulations.

Thus, the authors mentioned, and many other writers[1] on the cardiopneumatic movements, all agree, so far as I can see, that the movements are expressions of the variations of pressure within the air-tight thoracic cavity caused by changes either in the volume of the heart or in the volume of the blood contained in the thoracic cavity.

A recent article by Haycraft and Edie[2] opposes this view. These authors state that the cardiopneumatic movements "occur equally well with the chest cavity open and freely communicating with the outer air" (p. 429). It is obvious, therefore, they say, that the hypothesis of Ceradini and Landois can hardly be accepted as explaining the cardiopneumatic movements. They offer another hypothesis instead, namely, that the movements are "simply due to the heart pressing against the lungs, and that the lungs acted like an oncometer placed around it" (p. 430). The proof for this hypothesis they see in the fact that the cardiopneumatic movements almost entirely cease on lifting the heart away from the lungs. The writers are so thoroughly convinced of the correctness and simplicity of their position that they can hardly understand why it was overlooked by all the other writers on the subject, especially by Landois, who was the first one to obtain tracings of these movements. "It is a pity that he did not go a step or two further," they say, "their entire explanation must have dawned upon him" (p. 435).

The purpose of this Paper is to test the validity of the views advanced by Haycraft and Edie. Before entering into a further discussion, I wish, however, to remark that identical views were

[1] Loven: Nord. med. Ark., 1870, no. 19; P. Bert: Leçons sur la physiologie comparée de la respiration, Paris, 1870, p. 388: Von Brunn: Berliner klinische Wochenschrift, 1872, p. 130: Regnard: Revue mensuelle de médicine et de chirurgie, 1877, p. 333; Lépine: *ibid.*, p. 394; François-Franck: Travaux du laboratoire de Marey, 1877, p. 233.

[2] Haycraft and Edie: Journal of physiology, 1891, xii, p. 426.

advanced by Klemensiewicz [1] about fourteen years before Haycraft and Edie, just after the appearance of the monograph of Landois. The original article is not accessible to me, but there is a short report of it in the Jahresbericht of Hofmann und Schwalbe [2] which I will quote here in part. "Klemensiewicz reports experiments on the cardiopneumatic movements, which can also be seen in the frog. He rejects the explanation of Landois because the phenomenon is also present when the thorax is open. The movements are due rather to the intimate relation between the heart and the lungs, the latter, like a large Marey's tambour, registering all the movements and vibrations of the heart." We see here the same hypothesis as that of Haycraft and Edie, and also the same argument for rejection of the hypothesis of Landois and others. In discussing the new hypothesis and the arguments against the older one, I shall use the statements of Haycraft and Edie, as I do not know the experiments upon which Klemensiewicz has based his opinion.

According to Haycraft and Edie, the cardiopneumatic curve represents the variations in the pressure exerted by the heart upon the lungs. As the heart slowly changes its size during diastole, it presses upon the lungs and causes the gradual (expiratory) upstroke. In the beginning of the systole the heart at first "resents" its distortion by the lungs, — it "asserts" itself, which again causes a small but steep upstroke; then as it becomes smaller in all dimensions, it recedes from the lungs, which now expand, thus causing a sharp downstroke, — an inspiration. In a certain sense the theory of Haycraft and Edie coincides with the original hypothesis of Voit and Ceradini, inasmuch as both agree that the movements are due to the change of pressure caused by the change in the size of the heart; but while Voit and Ceradini meant the pressure exerted upon all the contents of the thoracic cavity, Haycraft and Edie mean only the direct pressure upon the lungs.

The interpretation of these authors, however, seems to me to be open to some criticism. We can understand why the pressure of the heart upon the lungs during diastole should produce an expiratory movement; we can admit the possibility that the "self-assertion" of

[1] Klemensiewicz, R.: Beiträge zur Demonstration des Pulses und Herzstosses mittelst der manometrischen Flamme, nebst Versuchen über die sog. cardiopneumatischen Bewegungen. Mitteilungen des Vereins der Aerzte im Steiermark, 1875-76.

[2] Jahresbericht über die Fortschritte der Anatomie und Physiologie, 1877, p. 56.

the heart will also cause a slight expiratory puff; but we cannot comprehend why the recession of the heart during systole should be followed by an inspiratory movement, — by an expansion of the lungs. Even in a state of collapse, the lungs are not perfectly atelectatic, but contain some air, and their elastic tissues are still stretched. When, now, air is driven out by the alleged pressure of the heart, expanding in diastole, what force is then present in the open chest that could distend the lungs anew against their own elastic tension, after they are released from the heart's pressure? In the tracings obtained from the lungs while the thorax is open, the apparent expansion of the lungs after the alleged diastolic pressure of the heart upon them has been withdrawn may be due to the elastic reaction of the rubber cover of Marey's tambour, which strives to return to its position of equilibrium after being stretched by the preceding expiration caused by the hypothetical pressure of the heart in diastole. But in the normal individual, in whom the elastic lungs are always considerably stretched, what could cause the lungs to expand again during systole against the strong pull of their elastic fibres; especially in such experiments as Landois and Ceradini made, in which the cardiopneumatic movements were demonstrated by the gas-flame and by smoke in a manometer? Smoke is lighter even than air, but, nevertheless, an inspiratory movement is seen in the smoke-column during each systole. What force except the negative pressure could compel the lung to follow the receding heart?

Again, Haycraft and Edie explain the entire cardiopneumatic curve also by the pressure of the heart upon the lungs, and do not permit the change in the pressure within the thorax to exert any influence upon it. But it is, nevertheless, an indisputable fact that during each cardiac cycle there is a considerable variation in the volume of blood present in the thorax. Now, why should this change of volume not cause a change of pressure in the normal, air-tight thorax, and why should this change of pressure not cause an expiration and inspiration, and leave a marked impression upon the cardiopneumatic curve? In this connection, it may be observed that Haycraft and Edie were not very fortunate in comparing the effect of the heart upon the lungs with the working of an oncometer. Here, too, the contractions of the organ enclosed within the oncometer are transmitted only by the changes in the negative pressure which they cause in the air-tight capsule of the instrument.

Furthermore, Haycraft and Edie in support of their statement that the open thorax has no influence upon the cardiopneumatic movements have published two figures, each containing two tracings, — one taken before and the other after the opening of the thorax. In both figures, however, the tracings taken when the thorax was open differ distinctly from those taken from the normal animal. I reproduce here one of these figures.

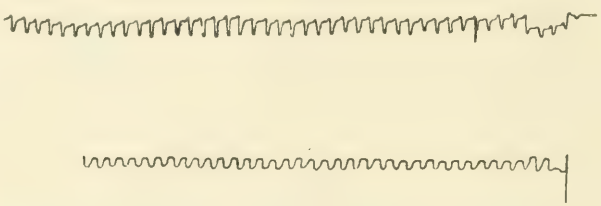


FIG. 1. (Fig. 4 in Haycraft and Edie's article; Journal of Physiology, 1891, xii, p. 431). "Tracing (1) was taken from a rabbit with its chest cavity in normal condition; tracing (2) after making a free opening into the cavity."

In order to gain a personal insight into this problem I have repeated the experiments of Haycraft and Edie. These authors do not tell us directly from what animals they derived their results. There is a remark in their article that they have experimented with the lungs of rabbits and sheep, but this has reference to another kind of experiments. It is said, however, that the tracings which they present were obtained from rabbits. I have therefore first experimented on rabbits. The method was in general the same as that employed by the authors mentioned and by Landois. The animals were given chloral and then curare, and were kept alive by artificial respiration. The tracheal cannula was connected with a Y tube, each limb being provided with a stop-cock. One limb was connected with the apparatus for artificial respiration, and the other with a Marey's tambour registering on a revolving cylinder. When the stop-cock leading to the apparatus for artificial respiration was closed and that leading to the Marey's tambour opened, the cardiopneumatic movements soon appeared. After taking a few tracings from the normal animal, the chest was opened and tracings were again taken. I repeated these experiments on eight rabbits, from every one of which I uniformly obtained the following result: when both pleural cavities were freely opened there was no cardiopneumatic oscillation on the tracing from the trachea.

Fig. 2 shows a part of the tracings taken just before and after the opening of the thorax. The tracing taken soon after both sides of the thorax were opened is simply a straight line, drawn from a lower level on account of the collapsed condition of the lungs.

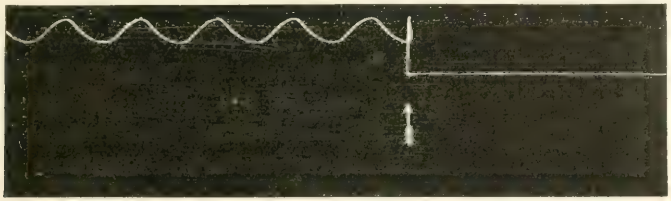


FIG. 2. The upper tracing is a cardiopneumogram from the trachea of a rabbit. On the left of the arrow are the cardiopneumograms taken while the chest was intact. After opening both pleural cavities all movements disappeared, and the tambour registered the straight line to the right of the arrow.

My results then were in direct contradiction to those described by Haycraft and Edie. I soon discovered, however, that there was a difference between the method of opening the thorax employed by Haycraft and Edie and that employed by myself. I usually opened each pleural cavity separately on their respective sides of the sternum. In one experiment in which I removed a part of the sternum some slight undulations could indeed be noticed on the tracing obtained from the trachea immediately after opening the chest (see Fig. 3).

Haycraft and Edie opened the abdominal cavity and cut away the anterior attachments of the diaphragm along with the anterior chest wall in its lower part. Of this method, which Haycraft calls the best,

FIG. 3. Cardiopneumatic tracing, from a rabbit. At *x* a part of the sternum was removed; some fine undulations are noticeable on the line to the right.

he himself speaks as follows: "As soon as this is done, the heart will fall down in its natural bed formed posteriorly by the lungs and will be carried up and down by them with the movements of respiration; it will be loosened from its more solid moorings to the chest wall and will be seen floating as it were upon the lungs. It is in this position that physiologists from Harvey's time onwards have chiefly

studied its movements, making, I think, too little allowance for the fact that the organ is in an entirely unnatural condition in respect to its attachment."[1] I think that Haycraft is correct in this, but that he and Edie themselves make too little allowance for the fact that in their experiments the heart was in an entirely unnatural condition with respect to its attachments. I have repeated their experiment also on a number of dogs, and have convinced myself more than once that when the pleural cavities are opened without disturbing the natural relations of the heart to the front wall and diaphragm, the cardiopneumatic movements disappear either entirely or are hardly perceptible. When, however, as in Fig. 3, the attachments to the sternum and the diaphragm are removed and the heart allowed to fall back upon the lungs, some distinct movements appear again.

The experiment illustrated by Fig. 4 shows us (1) that the opening of the thorax, without disturbing the natural attachments of the heart, nearly destroys the movements (see tracings Nos. 2 and 4); (2) that the closure of the opening in the chest, though surely not absolutely air-tight, brings the movements out again to a certain degree (tracings Nos. 3 and 6); (3) that the removal of the normal attachments of the heart causes the heart to fall back upon the lungs and brings out movements that seem to be different in size and character from those which occur when the chest is air-tight and intact (tracing No. 5).

There is still another point which deserves special comment. If the communication between the trachea and the Marey's tambour were established immediately after the artificial respiration is discontinued, the rubber cover of the tambour would be exposed to an abnormally high pressure by the air escaping from the inflated lungs. To avoid this I have regularly permitted the thorough escape of the air from the lungs before a tracing was taken. To attain this I placed a T-tube between the stop-cock on the limb leading to the apparatus for artificial respiration and the tracheal cannula; this tube had a stop-cock on its vertical limb which was kept slightly open during the artificial respiration, and which I might call "the relief stop-cock." Before taking a tracing the following order was observed. First the relief stop-cock was opened fully, then the stop-cock of the artificial respiration was closed and that leading to the tambour was opened; and, finally, after the lever of the tambour reached its nor-

[1] HAYCRAFT, J. B.: The movements of the heart within the chest-cavity and the cardiogram. Journal of physiology, 1891, xii, p. 447.

mal position again, the relief stop-cock was closed and a tracing taken. With these precautions the tambour was under an equal atmospheric pressure inside and outside while registering the movements. If the relief stop-cock was closed before all the surplus air had escaped, the lungs did not thoroughly collapse and the tambour registered some movements, although the thorax was open and the attachments of the heart thoroughly removed; the movements disappeared as

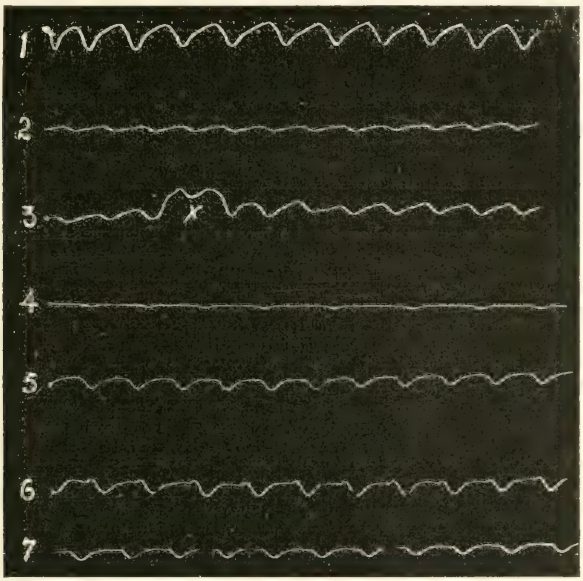


FIG. 4. (1) Shows the cardiopneumatic movements in a small dog with chest unopened. (2) Taken after the left pleural cavity was opened, the undulations becoming very small. (3) The continuation of tracing 2; closing the opening with a towel caused the movements to increase again. (4) Taken after both pleural cavities were opened; there is only a trace of the movements to be noticed. (5) Taken under the same conditions, but after the attachments of the heart to the front wall and the diaphragm had been thoroughly removed. The movements are again considerably increased, but they differ in character from the normal pneumocardiograms of the same dog, and resemble tracing 2 in Fig. 1 (from Haycraft and Edie, see above). (6) Taken under the conditions of tracing 5, but both openings were closed with towels. The size and especially the character is changed. (7) The towels were removed and the tracings are once more the same as in 5

soon as the air was permitted to escape thoroughly. These movements were quite large at times, especially when the attachments of the heart were thoroughly removed. The tracing in Fig. 5 illustrates this case.

While this tracing was being taken, both pleural cavities of the dog were wide open and the attachments of the heart removed, but the lungs were still considerably inflated and the heart was buried between them. The artificial respiration was interrupted for a long period; the dyspnœa caused a slowing of the beats of the heart, which, becoming quite large during each diastole, pressed the lungs to the sides of the thorax, and hereby caused large but not characteristic cardiopneumograms. Haycraft and Edie, it should be remarked, do not tell us what precautions they have taken to avoid

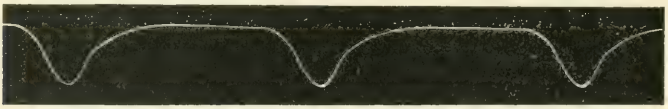


FIG. 5. Cardiopneumatic curve taken from a large dog. Dyspnœa; thorax wide open; attachments of heart thoroughly removed, but lung still quite inflated.

this artificial condition of affairs. We read there: "On stopping the respiration, opening the communication with the tambour, and clamping the tube passing to the bellows, the cardiopneumatic movements were well seen" (p. 430). I know by experience that even with an opening widely communicating with the air, it takes some time for an artificially ventilated lung to reach the limit of collapse. Haycraft and Edie do not tell us explicitly that they have taken the necessary precautions; perhaps the lungs of their animals still contained surplus air when the tracings were taken, giving them artificial cardiograms not to be obtained under normal conditions.

My experiments justify the following conclusions: —

(1) The cardiopneumatic movements disappear when both pleural cavities are open, provided the heart retains its normal attachments and the lungs are thoroughly collapsed before the tracings from the trachea are taken;

(2) The results of Haycraft and Edie might have been caused by their method of opening the thorax, which permits the falling back of the heart upon the lungs, and also might have been influenced by an incomplete collapse of the lungs;

(3) Without the assistance of the elasticity of the rubber cover of the tambour, the lungs in the open chest cannot follow the receding heart in the systole and no inspiratory movement can occur;

(4) The hypothesis offered by Haycraft and Edie that the lungs act like an "oncometer" placed around the heart cannot be accepted as an explanation of the normal cardiopneumatic movements.

For these reasons I agree with the majority of the writers that the cardiopneumatic movements have their origin in variations of the intrathoracic pressure caused by certain changes in the circulation.

CONTRIBUTIONS TO THE PHYSIOLOGY OF THE CARDIAC NERVES IN THE GUINEA-PIG.

By D. W. HARRINGTON, A.M., M.D.

[*From the Physiological Laboratory of Columbia University, at the College of Physicians and Surgeons, New York.*]

WHILE the guinea-pig has been used largely in experimental pathology, it seems to have been used little as yet in physiological research; in the literature to which I have had access I have noticed but two references to the physiology of the heart or of the cardiac nerves of this animal. In papers published by Legros and Onimus [1] and by MacWilliam [2] references are made to the effect upon the heart of stimulating the vagus nerve in the guinea-pig; it is evident, however, that their experiments upon this animal were very limited in number. The fact that the guinea-pig is used so extensively in experimental pathology may give some interest to the experiments described in this paper.

I. Method of Experimenting.

The guinea-pigs used in these experiments were of various sizes; the average weight, however, was 584 grams. Animals of both sexes and of various ages were used.

Anæsthetics. The animals were thoroughly anæsthetized in all cases. The anæsthetics used in the various experiments were ether, given by inhalation; chloral hydrate, opium, and morphine, these three given subcutaneously, either singly or in various combinations. When chloral was used alone, 0.5 gram was given a short time before beginning the operation. Smaller doses were given as required during the experiment. Of opium and chloral I have used 1 cubic centimetre of the deodorized tincture of opium combined with 0.25 gram of chloral; of morphine and chloral I have used 0.005 gram of morphine combined with 0.25 gram of chloral. It is usually advisable to give a little ether by inhalation while the dissection is performed.

[1] Legros et Onimus: Journal de l'anatomie et de la physiologie, 1872, pp. 575 and 578.

[2] MacWilliam: Journal of physiology, 1888, ix. p. 387

Recording of blood-pressure. The blood-pressure was measured by means of a cannula inserted into the proximal stump of one of the carotid arteries. As the arteries of the guinea-pig are very small and the tissues very delicate, the insertion of a cannula into one of the carotids frequently offers difficulties. The following method was found to be of great assistance in performing this operation. After the artery had been dissected from the sheath it was clamped and divided and a fine silk thread was tied to the proximal stump just above the point at which the opening in the artery for the cannula was to be made. The artery was then lifted from the wound and slightly stretched, and the thread attached to the artery was held in the operator's teeth, — a procedure which left one hand free for the use of the forceps and the other to hold the cannula. Moreover, taking the thread in the teeth seems to inhibit the ordinary reflexes of the operator's body and thus he is better enabled to work with a steady hand. The blood-pressure was recorded by a mercurial manometer on the smoked paper of a drum-kymograph, the fineness of the tracing usually obtained being too great for the use of ink to be satisfactory. For excitation of the nerves the faradic current of an ordinary du Bois-Reymond induction coil was used; the current for the primary coil was obtained from an electric-light dynamo, and was maintained at a little less than one ampère, by throwing in the necessary amount of resistance. The interruption of the primary current was by Neef's electro-magnetic hammer. Small shielded electrodes of platinum were used.

Normal blood-pressure. The average mean blood-pressure (corrected for the weight of the solution of sodium carbonate) as determined upon guinea-pigs anæsthetized by one or more of the above-mentioned drugs, was 75 millimetres of mercury; the highest blood-pressure observed was 111 mm., the lowest, 56 mm. The average rate of the heart-beat was 200 per minute, the fastest and slowest rates observed being 288 and 132 respectively. The average number of respirations per minute of animals quiet in their cage (the temperature of the room being 20° C.) was 72 per minute.

II. The Vagus Nerve.

The vagi were investigated after exposure in the neck, where they occupy about the same anatomical position in the guinea-pig as in other mammals.

Section of the vagi. Section of both vagi in the guinea-pig seems to have little effect upon either the rate of the heart or the blood-pressure. In a few cases slight acceleration was noticed for a short time after the section; but this usually gave place, within ten or twenty seconds, to the normal rate. Much more frequently section was followed by a slight slowing of the rate of the heart during the first ten seconds, this probably being caused by mechanical stimulation of the inhibitory fibres. In no case was a rise of blood-pressure observed to follow section of both vagi. Thus the inhibitory nerves of the heart of the guinea-pig do not seem to be in constant activity.

Stimulation of the vagus; effect of the season upon the result. Meyer has shown that the effect upon the heart of stimulation of the vagus nerve is much more marked in the cold-blooded animals than in the warm-blooded ones, and other investigators have confirmed Meyer's conclusions.[1] Since vagus inhibition is less effective in the case of the more frequently beating hearts of warm-blooded animals, the question naturally suggests itself whether in such hearts as that of the guinea-pig, of which the average number of pulsations per minute is 200, the inhibitory power of the vagi is sufficient to bring the heart to a standstill.

My work on the guinea-pig was begun in October, 1896. It was suspended during November and December and resumed in January, 1897. It was continued through January, February, March, and April. For convenience the time may be divided into two periods, an early period, from October until the end of January, and a later period, including the latter part of February, March, and April. During each of these two periods the results of vagus stimulation differed quite markedly from the results obtained during the other period, the curve of inhibition being characteristic of the period in which it was taken. During the first period, *i. e.*, from October to January, cardiac inhibition from excitation of the vagi was much less marked than during the second period from February to April. In no case during the first period was I able to bring the heart to a standstill, no matter how strong a current was applied to the vagus, and I came to the conclusion that in at least one of the warm-blooded animals with a very frequently beating heart, *i. e.*, the guinea-pig, the inhibitory power of the vagus was not sufficient to bring the heart to a standstill. During the first weeks in February, however, I was surprised to find that in one guinea-pig the heart was stopped by a faradic current

[1] See HOUGH: Journal of physiology, 1895, xviii. p. 161.

of only moderate strength. For a short time after this I noticed that in some guinea-pigs the heart was stopped by a moderately strong current (the secondary coil being at about 10 cm.), whereas in others the strongest current used (the secondary coil being at 0 cm.) was unable to stop it. During the latter part of February and throughout March and April the heart was invariably brought to a standstill by faradic currents of the strength commonly used in physiological work, *i. e.*, just perceptible when applied to the tongue. In some cases very weak currents, such as are obtained when the secondary coil stands at 24, 28, and 30 centimetres from the primary, sufficed to cause stoppage.

The curves of inhibition obtained during the first period differed in several respects from those obtained during the second period. In the former (see Fig. 1) the slowing of the heart and the fall of blood-

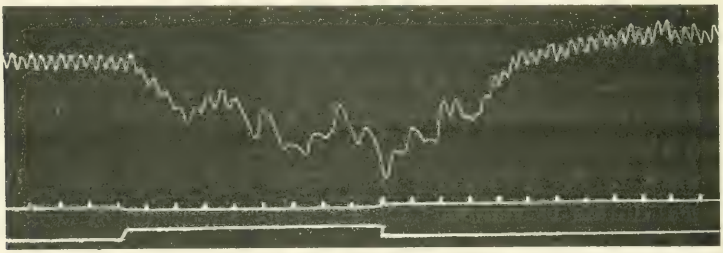


FIGURE 1. Inhibition from stimulation of the left vagus, with the secondary coil at 5 cm. Time in seconds. The line of zero pressure is not shown. The writing-points of the manometer and of the stimulating key were in the same vertical line.

pressure were gradual; the fall of pressure was not very great in proportion to the normal blood-pressure, which as a rule was considerably higher during the first than during the second period. The return of the blood-pressure and the heart-rate to the normal, after the cessation of stimulation, was gradual and fairly regular, and inhibition was followed by comparatively little irregularity of heart-rate or of blood-pressure. On the other hand, during the second period the stopping of the heart and the fall of blood-pressure were sudden, the descent in the curve being sometimes almost vertical (see Fig. 2). The blood-pressure was very irregular after the cessation of stimulation, sometimes failing to return to the ordinary height, while more frequently it rose far above it and then gradually returned to it or fell below it.

At about the season when it was first noticed that excitation of the vagus was bringing the heart to a standstill, it was also noticed that the guinea-pigs under experiment did not live as long as they had formerly done. Later it was noticed that they died very easily, and without any apparent cause; no sooner were the necessary dissections made, and the artery connected with the manometer, than the animal died. Although the anæsthetics were used with great care, and various ones were tried, there was no improvement. At the season in question the dissection was done more carefully and more rapidly than during October, and everything pertaining to the operation was more favorable than during the earlier months; still the animals died before any results of value could be obtained. In many cases the tissues of the neck showed an unduly venous condition of the blood before the cannula was inserted into the artery; respiration ceased; the heart

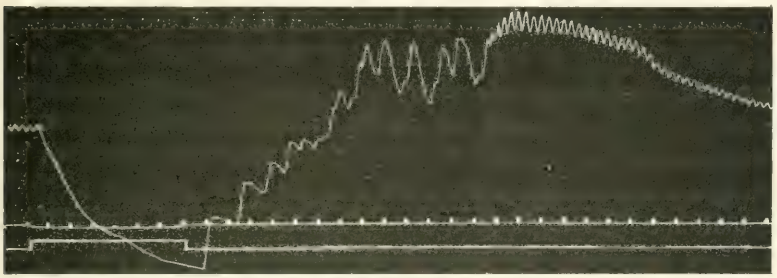


FIGURE 2. Four-fifths the original size. Inhibition from stimulation of the left vagus with the secondary coil at 16 cm. Time in seconds. The line of zero pressure is not shown. The writing-points of the manometer and of the stimulating key were in the same vertical line.

became feeble, and the animal died. The heart usually continued to beat for a short time after respiration had ceased; artificial respiration, however, did not prolong the life of the animal. In April it became practically impossible to get any results whatever from the experiments. In order to be certain that the trouble was not wholly with the special lot of animals on hand, or with the hygienic conditions to which they were exposed, a new lot of animals was procured, but the results were not improved except in a few cases. The only possible explanation of these results seems to be that the lack of vitality was due either to some unknown cause associated with the season of the year, or to the diminution of fresh air and light during the winter months, or to both causes combined. Nearly every one has

experienced in his own person a certain diminution of vitality during the spring months. It is a well-known fact that persons suffering from chronic diseases are much more liable to die during March and April than during other months of the year; and eminent surgeons state that major operations are more liable to be followed by death during those months than at other seasons. There would seem, however, to be some slight evidence in favor of the view that diminution of fresh air and light during the winter months is partially responsible for this lack of vitality in the guinea-pigs, from the fact that, of the last lot of the guinea-pigs used, a few, which had been placed in the sunlight in a specially well ventilated room for two weeks, showed greater vitality than those of the same lot kept elsewhere, although much less vitality than those subjected to experiment from October to January. Hygienic influences alone, however, do not suffice to explain the differences of vitality observed.

It seems clear from what has been said that, in the guinea-pig at least, the efficiency of the stimulation of the inhibitory nerves of the heart is inversely proportional to the degree of vitality possessed by the animal. In a measure this agrees with the opinion expressed by Hough,[1] who states that in his experiments upon cats, when the heart from any cause has been weakened and the pulse has become feeble, stimulation of the vagi has been much more effective than when the heart was vigorous; the slowing of the heart and the fall of blood-pressure being much more pronounced. I did not find, however, that in the guinea-pig when the heart had been weakened from profound anæsthesia, from shock, or from loss of blood, stimulation of the vagi was more efficient, for in no case during the earlier period, from October to January, no matter what was the condition of the animal, did stimulation of the vagi stop the heart. Hough states that in the cat the heart can rarely be brought to a complete standstill, not oftener, I think, than once in twenty cases. I do not know at what season of the year his experiments were made, or in what conditions the animals upon which he operated were kept, but in two of three experiments upon cats which I made in April the heart was brought to a standstill and maintained at a standstill for periods of half a minute when the vagus was stimulated with a faradic current of moderate strength.

After-effects of stimulation of one vagus. After the cessation of a stimulation of the vagus during which the heart had been slowed or

[1] Hough: *op. cit.*, p. 164.

brought to a standstill, the beat usually returned quickly to its previous rate, and there was neither a secondary acceleration, as is often observed when the vagus of the dog has been stimulated, nor a long-continued slowing, such as occurs frequently when the vagus of the opossum [1] has been stimulated. The blood-pressure after stimulation of the vagus was, however, often very irregular; this irregularity was much more marked in the spring than in the autumn or winter months. These irregularities of the blood-pressure were frequently accompanied by irregularities of the heart-rate.

During the months of the spring, however, there sometimes occurred even before stimulation, and without any apparent cause, marked irregularities of the blood-pressure and the heart-rate, whereas during the autumn months one of the most striking characteristics of the tracing had been the great regularity of the blood-pressure and of the heart-rate; as a rule, the latter varied very little in the course of a long experiment, but continued almost the same till the animal was at the point of death. In fact, during the spring months there seemed to be a want of stability or of general tone on the part of the heart and perhaps of the vaso-motor system, a condition which seems to me to resemble that which I have observed in frogs in the spring, when studying the form of the muscle-curve with the pendulum-myograph: the muscle-curves being very irregular although the conditions of the experiments were kept as nearly constant as possible.

Rise of blood-pressure following stimulation of the vagus. At times, after the cessation of a stimulation of the vagus in the guinea-pig, the blood-pressure rose far above its original height (see Figs. 2 and 3); in one case it was doubled. The cause of such a marked rise of blood-pressure following inhibition deserves investigation. One explanation of this phenomenon which might be suggested is that the vagus nerve is the trophic nerve of the heart, that stimulation of this nerve causes constructive metabolism to be induced during the period of inhibition, and that the heart is thus "nursed into more vigorous activity." The "good effects" upon the heart of vagus inhibition artificially induced in the warm-blooded animals may, I think, be questioned. My experience with the guinea-pig would seem to support the view that caution should be used in drawing very detailed conclusions with regard to specific physiological conditions in one kind of animals from experimental work on animals very

[1] Hunt and Harrington: Journal of experimental medicine, 1897, ii, p. 715.

different morphologically and, in general, physiologically. The infrequently beating hearts of the cold-blooded frog and turtle are very different in several respects from the frequently beating hearts of the warm-blooded rabbit and guinea-pig. The opinion that inhibition caused by vagus stimulation is beneficial to the heart is largely the

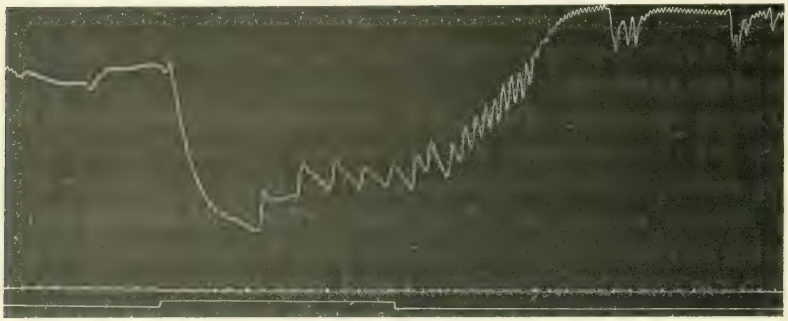


FIGURE 3. Three-fifths the original size. Inhibition from stimulation of the right vagus of the guinea-pig with the secondary coil at 15 cm. Time in seconds. The line of zero pressure is not shown. The writing-points of the manometer and of the stimulating key were in the same vertical line.

result of the teaching of Gaskell, but it must be remembered that Gaskell concludes his paper [1] by stating that his observations were confined to the cold-blooded animals, and that he is "not yet in position to say how far, in the more highly-developed mammalia, the phenomena of the heart may have become changed under a greater differentiation of function, and an increased complexity of structure." Immediate supply of nutriment is a matter of comparatively little importance to the cold-blooded hearts; it is a matter of the greatest importance to the very frequently beating warm-blooded hearts. "The two organs of the body whose supply of oxygenated blood cannot be interrupted, even temporarily, without danger to the system are the central nervous system and the heart." [2] "The force of the ventricular contraction is immediately affected by a change in the amount of blood supplied to the cardiac muscle," [3] and "more important than the quantity is the quality of the blood flowing through

[1] GASKELL: Journal of physiology, 1883, iv, p. 124.

[2] ROY and ADAMI: Philosophical transactions, 1892, clxxxiii, B, p. 290.

[3] MAGRATH and KENNEDY: Journal of experimental medicine, 1897, ii, pp. 13, 14.

the coronary vessels."[1] During any prolonged period of cardiac inhibition with a fall of blood-pressure in the aorta, the supply of nutriment to the heart muscle must certainly be diminished, and, as the right side of the heart is inhibited as well as the left, the arterialization of the blood must be diminished as well, and hence its quality deteriorated. So it seems very probable that any good effects upon the heart due to stimulation of trophic fibres may easily be counterbalanced by the injurious effects just pointed out. Hence a sudden and marked rise of pressure following inhibition is very probably due to some cause other than improvement in the nutrition of the heart. Moreover, this rise probably is not due to stimulation of the vasoconstrictor centre by a too venous condition of the blood; the rise occurs too suddenly to admit of such an explanation.

Whatever may prove to be the correct explanation of a rise of blood-pressure in some guinea-pigs after stimulation of the vagus, this rise is almost invariably followed immediately by a fall of blood-pressure below the normal, and very frequently by sudden failure of the heart and death of the animal. Fig. 3 is a tracing showing cardiac inhibition from stimulation of the vagus immediately after the animal had been prepared. After the cessation of the stimulation there took place a considerable rise of blood-pressure; the heart's beat became irregular, and the animal died within two minutes, death being preceded by a very rapid fall of blood-pressure. Throughout the whole series of my experiments stimulation of the vagi seemed to lessen the efficiency of the heart. This was especially true in the months from February to April, when the vitality of the animals was low, but it was also true in the months from October to January.

"*Escape*" *of the heart from vagus stimulation.* The heart of a guinea-pig when brought to a standstill by stimulation of the vagus soon begins to beat again; or, when slowed, to increase the frequency of its beats. The longest period during which I was able to maintain a standstill by stimulating the vagus was twenty-one seconds, and in this case death followed almost immediately, as was usually the case when the vagus nerve had been stimulated for any length of time in the spring. The following experiments illustrate the rate of escape during that season. I have no record of escape during the autumn, when the animals were in a more vigorous condition.

[1] FOSTER: Text-book of physiology, 6th ed., 1893, p. 367.

Experiment I. Guinea-pig; weight 550 grams; corrected mean blood-pressure 69 mm. of mercury; normal heart-rate 32 (all of the rates given are for periods of 10 seconds); peripheral end of right vagus stimulated while the secondary coil was at 15 cm. Rates during stimulation: $6\frac{1}{2}$, 9, 15, 16, 8, 6, death.

Experiment II. Guinea-pig; weight 637 grams; corrected mean blood-pressure 84 mm.; normal heart-rate 38; peripheral end of right vagus stimulated, secondary coil at 10 cm. Rates during stimulation: 3, 17, 15, 19, 25, 31, 35. The heart failed suddenly after the rate had increased to 35 and the blood-pressure had nearly reached the normal.

Effect of shunting the current from one vagus nerve to the other. It is an interesting question whether there be a single inhibitory mechanism in the heart or one for each vagus nerve. It is believed by many [1] that the same intracardiac apparatus serves for both nerves, — that after the heart of a mammal has begun to escape from inhibition produced by stimulation of one nerve, shunting the current into the other nerve does not cause a second standstill. I have found the contrary to be true in the guinea-pig, and have repeatedly caused a second standstill by suddenly shunting the current into the second nerve after escape had commenced from the inhibition caused by continued stimulation of the first nerve. This was tried, however, only in the spring months, when the cardiac-inhibitory mechanism was perhaps unusually irritable.

The following case has several features of interest: —

February 22, 1897. Guinea-pig; weight 510 grams. Chloral and morphine. Corrected mean blood-pressure 83 mm.; pulse-rate 37 in 10 seconds. Both vagi cut. Secondary coil at 12 cm. Stimulation of peripheral end of left vagus; heart stopped 10 seconds and blood-pressure fell to 26 mm.; heart's rate increased to 5 beats in 10 seconds and blood-pressure rose to 53 mm.; current shunted to right nerve; heart stopped 11 seconds and blood-pressure again fell to about 26 mm. The heart then rapidly increased in rate (the stimulation still continuing), gave a few irregular beats, and suddenly increased to 55 beats in 10 seconds, while the rate before stimulation had been only 37. Following a short period (12 seconds) of frequent beating, there occurred a period of infrequent irregular pulsations alternating with frequent beats. This state of things was allowed to continue for half a minute, when the current was shunted back into the left nerve; the heart was again stopped for four seconds. The heart's rate suddenly increased to 42 in 10 seconds,

[1] Hüfler, E.: Die abgestufte Reizung des Herzvagus. Archiv für Physiologie, 1880, p. 295. Hough, *op. cit.*, p. 198.

when a short period of frequent and irregular beating was followed by failure of the heart and death of the animal, the stimulation having been maintained to the end. This is the only case in which acceleration was observed to occur during continued stimulation of the vagus. It is the only case in which acceleration was observed, except a few cases in which it appeared as an after-effect of inhibition.

The comparative efficiency of the two vagi. In a number of species of animals one vagus, usually the right, has been found to exert a more powerful influence upon the heart than does the other. In the guinea-pig I have found both vagi to be always efficient, and in no case have I been able to discover any greater efficiency on the part of one than on that of the other.

In quite a number of cases simultaneous stimulation of both vagi has not been observed to give more powerful inhibition than stimulation of the same strength applied to either nerve separately.

III. The Depressor Nerve.

There is found in the guinea-pig in close relation to the vagus and cervical sympathetic a very delicate nerve, stimulation of which causes a fall of blood-pressure resembling in every respect that caused by stimulating the depressor in the rabbit. This nerve can usually be found by raising the carotid artery out of its sheath on a curved

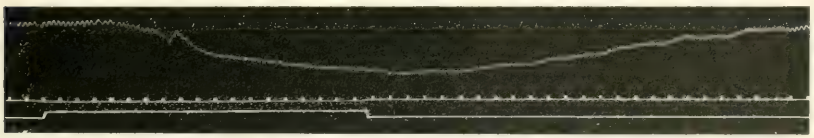


Figure 4. Three-fifths original size. Fall of blood-pressure as a result of stimulation of the central end of the left depressor with the secondary coil at 8 cm. Time in seconds. The line of zero pressure is not shown. The writing-points of the manometer and of the stimulating key were in the same vertical line.

needle and thus putting the tissues between the carotid and the vagus on the stretch, the nerve is then seen extending through the connective tissue as a delicate whitish filament. At least part of this nerve can be traced to the ganglion of the trunk of the vagus, and in so far its origin resembles that of the depressor in the opossum;[1] whether, as in the opossum, there is a second root springing from the superior laryngeal nerve I have not been able to determine satisfactorily.

[1] Hunt and Harrington: *op. cit.*, p. 717.

Stimulation of the central end of this nerve gives results very similar to those observed when the depressor of the rabbit or of the opossum is stimulated, namely, a fall of blood-pressure (Fig. 4) and moderate slowing of the heart's rate if the vagi are intact.

A number of attempts were made to stimulate the various branches of the stellate ganglion to determine whether they contained cardiac accelerator nerves, but as this work was deferred until the spring, it was found that the animals did not possess sufficient vitality to permit the necessary dissection and prolonged experiment.

In conclusion I desire to express my indebtedness for valuable assistance and suggestions to Professor Frederic S. Lee and to Dr. Reid Hunt.

THE RESTORATION OF COÖRDINATED, VOLITIONAL MOVEMENT AFTER NERVE "CROSSING."

By R. H. CUNNINGHAM, M.D.

[*Demonstrator of Physiology, College of Physicians and Surgeons, Columbia University, New York.*]

A CURSORY glance at a tabulated list of the voluminous literature[1] treating of the union of nerves after division will indicate that many eminent experimental investigators have zealously re-studied and discussed this subject ever since the historical experimental results of Cruickshank[2] were announced.

An analysis of this voluminous physiological and surgical literature fully substantiates the present consensus of opinion that if the cut ends of the central and peripheral portions of a recently divided mixed nerve be brought into apposition, complete restoration of function may ultimately occur in the peripheral portion. Further, the results of a number of physiologists (Flourens,[3] Bidder,[4] Schiff,[5] Philippeau and Vulpian,[6] Reichert,[7] Howell and Huber,[8] and others) indicate that if the central end of one divided mixed nerve be sutured to the peripheral end of another mixed nerve, union of the two ends may ultimately occur, and the function of the nerve fibres of the peripheral portion be re-established. That is to say, the nerve fibres composing the peripheral portion regain their function of conductivity as well as the property of irritability. Degenerated muscle fibres

[1] For the full bibliography of this subject to 1892 the reader is referred to the paper of Howell and Huber, Journal of physiology, 1892, xiii, p. 335.

[2] CRUICKSHANK: Philosophical transactions, 1795, xvii. See also FONTANA'S description (Sur le venin de la vipère, etc., Florence, 1781, p. 177) of Cruickshank's experiments.

[3] FLOURENS: Recherches expérimentales sur les propriétés et les fonctions du système nerveux, 1824, p. 272.

[4] BIDDER: Archiv für Anat., Physiol., und wissensch. Medicin, 1842, p. 102; Archiv für Anat. u. Physiol., 1865, p. 246.

[5] SCHIFF: Journal de la physiologie, 1860, iii, p. 217.

[6] PHILIPPEAU and VULPIAN: Journal de la physiologie, 1864, vi, p. 421 and 474.

[7] REICHERT, E. T.: American journal of the medical sciences, 1885, January.

[8] HOWELL and HUBER: Journal of physiology, 1892, xiii, p. 335; 1893, xiv, p. 1.

innervated by the peripheral portion of the nerve also regenerate and again contract to the stimulus of a nerve impulse.

If successful union of crossed nerves can be obtained, it is evident that when the motor nerve (N) of a group of muscles (M) has united to the peripheral portion of a motor nerve (n) of a group of muscles (m), and *vice versa*, the group of muscles (m) must receive their nerve impulses from that group of spinal nerve cells from which the nerve impulses to the group of muscles (M) formerly emanated. Similarly, the cells of origin of the nerve (n) will supply the nerve impulses to the muscles (M). Although a very decided change in the destination of the impulses from the spinal cells of origin of the two nerves has been produced by the crossing, the central relations of those spinal cells with each other, with other groups of cells, and with the neuraxons of the cells of the cerebral cortex have not been anatomically altered by simple division and suture of the peripheral nerve trunks.

Modern histological methods reveal, to some degree at least, how intricate and how wide-reaching are the connections which exist between the various central nervous mechanisms. Naturally, therefore, the old question investigated long ago by Flourens again arises as to whether, or no, the intricately connected central nervous mechanisms are in reality capable of adjusting themselves to the new state of affairs, so that the individual regains complete coördinate control of the muscles supplied by the crossed nerves. Further, if the nerve to a group of muscles which are rhythmically contracting and relaxing in response to rhythmical nerve impulses discharged by a certain group of nerve cells in the medulla or in the spinal cord, be divided and crossed with the central portion of another motor nerve, will the nerve cells from which the axis cylinders of the latter arise ultimately become a rhythmically discharging group and entirely assume the function of the rhythmically discharging cells after the regeneration of the united crossed nerves and muscles?

With a view of obtaining a definite answer to the two preceding questions, the various experiments described in this paper were performed.

Previous Work on the Subject. — Although various authors, following in the footsteps of Flourens, have divided and crossed different nerve trunks, motor nerves to supposedly sensory nerves and *vice versa*, and mixed nerves to other mixed nerves, none of these authors has investigated the muscular movements that occur in an animal's leg

with crossed nerves when the motor cortex is electrically or otherwise stimulated. Nor do they appear to have studied the effects upon the rhythmical respiratory and other movements of the vocal cords that may follow the crossing of one recurrens with another motor nerve. Most of the earlier investigators busied themselves with the solution of the problem as to whether, or no, sensory nerves would unite to motor nerves and *vice versa*, with the ultimate re-establishment of the function of the united portions. It is almost needless to point out that the results of such attempts do not come within the scope of this paper. Consequently I confine myself to a brief review of those previous observations that more directly bear upon a part of my own experiments.

According to Flourens'[1] description of his celebrated experiments, the two principal trunks of the brachial plexus in a cock were cut, and the peripheral end of the trunk supplying the upper surface of the wing was sutured to the central end of the other trunk, supplying the lower surface of the wing. At the end of several months the bird had regained perfect use of the extremity of the wing, which no longer dragged, and served for flying (?) as well as before the experiment. When the nerves were exposed, they had completely united in the order in which they had been placed, the inferior end of one nerve being continuous with the superior end of the other, and *vice versa*. In describing the physiological investigation of these united nerves, Flourens writes:[2] "I pinched the nerves above the point of their reunion, — the wing moved at once, and the animal cried; I pinched them below, and the animal felt it as before, and his wing moved again; the same thing took place, when I pinched the enlarged point of reunion. And further, when I pinched the superior nerve above the point of reunion, the muscles of the lower surface of the wing contracted; and, on the contrary, the muscles of the upper surface of the wing contracted when I pinched the inferior nerve, — always above the point of reunion."

[1] Flourens: *loc. cit.*

[2] "Je pinçai ces nerfs *au-dessus* du point de leur réunion, l'aile se mut aussitôt, et l'animal cria; je les pinçai *au-dessous*, l'animal le sentit de même, et son aile se mut encore; pareille chose eut lieu, quand je pinçai le *point grossi* de la réunion. Et de plus, quand je pinçais le nerf supérieur *au-dessus du point de la réunion*, c'étaient les muscles de la face inférieure de l'aile qui se contractaient; et c'était, au contraire, les muscles de la face supérieure de l'aile qui se contractaient quand je pinçais le nerf inferieur, toujours *au-dessus du point de la réunion*."

While this result of Flourens appears to be all that one could desire, the observer neglects to state whether the action of the tensors of the patagium, the nerves of which were probably not divided, was taken into consideration and properly excluded. No mention is made of a microscopical, or even of a very careful anatomical examination of the tissue between the necessarily adjacent crossed trunks. If the central and peripheral ends of the nerves in reality united with each other without the formation of a single nerve fibre between the two adjacent points of suture, the fact is all the more remarkable, for no special precautions seem to have been taken at the primary operation to prevent the latter occurrence, although such a new formation will invariably occur, according to the experience of the writer, unless prevented by some such method as is described below.

In other cocks and in a duck, Flourens sutured the central end of the fifth cervical nerve to the peripheral end of the divided vagus, and, after the expiration of a number of months, divided the other vagus. All the birds died in from one to four days after the latter operation. Information regarding the return of irritability to the united nerves is not given, but evidently the vagal functions had not been re-established *via* the nucleus of the fifth cervical nerve.

The experiments on dogs by Philippeau and Vulpian,[1] in which the central end of the vagus was crossed with the peripheral end of the hypoglossal and *vice versa*, only tend to show that mixed nerves of different origin are capable of union, and throw no light upon the positive restitution of voluntary coördinate control of the groups of muscles supplied by the above mentioned nerves. These observers concluded that although the central end of the vagus would unite to the peripheral end of the hypoglossus, the nerve fibres of the peripheral part of the hypoglossus would not recover their connections with their exciting nerve-centre, and the hypoglossus would be but an instrument at the command of the functional centre of the motor fibres contained in the cervical part of the vagus; a conclusion that seems to be substantiated by the results of the later experiments of Reichert.[2]

After suturing in five dogs the central end of one vagus to the peripheral end of the hypoglossus, Reichert found, after the nerves had

[1] Philippeau and Vulpian: Journal de la physiologie, 1864, p. 421.

[2] Reichert, E. T.: American journal of medical sciences, 1885, January.

united, that certain areas were present in the partially atrophied half of the tongue, which contracted synchronously with inspiration or with expiration, and concluded that the motor fibres of the vagus had actually become united to similar fibres in the trunk of the hypoglossal, and that the hypoglossal fibres conveyed impulses which were peculiar to the vagus apparatus.

Rawa[1] has obtained such remarkably incredible results after crossing nerves of different destination, and also nerves of special function, that one would naturally suspect that his observations and methods must be faulty. For instance, we are told in regard to the cats in which the hypoglossus was sutured to the vagus and *vice versa*, "that of the entire number of cats only six survived. Four of these cats (Nos. 4, 7, 9, 10) had the left central stump of the hypoglossus sutured to the peripheral vagus; two, a similar crossing of the nerves on the right side. In two other cats (12 and 14) the central vagus was sutured to the peripheral hypoglossus on the left side, and in cat No. 16 on the right side." At the expiration of 16–20 months, the right vagus was cut in cats 4 and 7, and both animals promptly died within five days. In cat 12, section of the opposite hypoglossal nerve was followed by loss of power to move the tongue. In cat 16, after the opposite hypoglossal was cut, no movements of the tongue were present, but in a few days the tongue was slowly moved, being contracted to the left, but the animal was killed at the end of six weeks. On page 310, cats 9, 10, and 11 are said to have died very shortly after the primary operation, although cats 9 and 10 were previously included among the six (?) cats that survived the section of one vagus. Likewise, one finds that cat No. 8, previously unincluded in the number of cats surviving the section of the right vagus, was operated on 16–20 months after the primary operation, and two centimetres of the left vagus were excised. Five days later, fearing to lose the animal, it was used for an experiment, for the details of which the reader is referred to the original paper. Rawa's experience leads him to conclude that (1) "after the peripheral portion of a nerve supplying a certain muscle has united to the central end of a nerve that supplies another muscle, the function of the former muscle becomes restored. (2) The direction of the voluntary motor impulses may be altered as one pleases, and the impulses will always accommodate themselves to the peripheral nerve endings." As a result of his experiments in crossing the hypoglossal and vagus, he

[1] Rawa: Archiv fur Physiologie, 1885, p. 296.

likewise concludes, "that the central nervous mechanisms can innervate organs that formerly did not connect with them, as soon as those organs become connected to them by nervous conductors." "Nerve centres will, by practice, supply exactly what the peripheral organs with which they became connected require of them."

Howell and Huber[1] crossed the ulnar and the median nerves in dogs and succeeded in getting the crossed nerves to unite without the formation of a cicatrix, common to all the ends. They found, to quote these observers verbatim, "that at the second day after the operation, with both median and ulnar cut on the left side high in the arm, and with the ulnar cut on the right side at the level of the elbow, there was very little evidence of any paralysis or even awkwardness." "Before the end of the first week the animal was running around in perfect freedom, and the closest scrutiny could detect no awkwardness of movement except possibly in running rapidly up stairs he would frequently stumble with his front feet; but whether this was due to the unusual innervation of the muscles, or was caused by the over-zealous activity characteristic of young dogs generally, could not be determined." The close relation between the origin and distribution of the median and ulnar nerves led these observers to remark that "a more interesting suture would probably be one between the musculo-spiral and ulnar in which centres of origin of extensor fibres would be obliged to innervate flexor muscles." They considered there was no histological or physiological obstacle to such a union, but considerable awkwardness of movement in the beginning might attend the functional use of the nerve by the animal. Judging, therefore, from the results of Howell and Huber it would appear that such nerves as the ulnar and the median, which innervate in the dog synergic groups of muscles, are not the ones to choose for crossing when it is desired to investigate the return of voluntary coördinated movements in muscles innervated by crossed nerves. The suture of two nerves supplying antagonistic groups of muscles will yield results that can be more accurately interpreted.

From the preceding brief historical review it is evident that there is room for considerable doubt as to whether the central nervous mechanisms concerned in volition and coördination will in reality adjust their nervous discharges so that a grown animal will regain full control of antagonistically acting groups of muscles after their nerve trunks have been crossed.

[1] Howell and Huber: Journal of physiology, 1892, xiii, p. 335.

Methods.— All the successful experiments were performed upon dogs. In two monkeys which I had hoped would prove more suitable than dogs for this variety of experiment, the ulnar and the median nerves were crossed with the musculo-spiral nerve, but as the experiments were not a success, no further mention need be made of them. Ether anæsthesia was employed for every operation, and all the operations except the last were performed with the strictest aseptic and antiseptic precautions. After the cerebral cortex, etc., had been investigated at the final operation, the animals were killed with an overdose of the anæsthetic.

The nerves were divided with a sharp razor and sutured with fine catgut prepared by the writer's formalin method.[1] Usually two to four fine sutures were employed. After the crossed nerves had been sutured, broad pieces of fascia covering the neighboring pectoral and other muscles were dissected off, and both of the apposed crossed nerves were gently wrapped, for about three-quarters of an inch above and below the point of suture, in separate pieces of this thin tissue, which was then sutured with fine catgut sutures to the fascia of the adjacent muscles. In all the experiments upon the ulnar, median, and musculo-spiral nerves, the common branch from the musculo-cutaneous nerve to the median was entirely excised, its point of origin from the musculo-cutaneous being ligated with a silk ligature. The wound was sutured with No. 2 catgut, dressed with bichloride of mercury gauze, the whole limb wrapped in cotton, bandaged, and, finally, put in plaster of Paris. The plaster not only encased the toes, but also covered the shoulder, and passed around the upper part of the thorax and the lower part of the neck. The fore limb was thus kept perfectly at rest for at least three weeks. The plaster bandage was then removed, to be immediately replaced by a clean one that was allowed to remain on the dog for four to six weeks. If any tendency to ulceration became evident after the removal of the plaster, it was again applied for two to four weeks, or longer, until the vitality of the tissues had sufficiently recovered to resist external sources of irritation. Consequently, by carefully protecting the peripheral parts, the majority of the dogs did not exhibit the ulcerative disturbances that are very liable to occur in the unprotected skin of the wrist, toes, etc., after division of the chief nerve supply of that region.

Previous to the operation, it was found that many of the dogs

[1] CUNNINGHAM: New York medical journal, 1895, April 20.

would give the paw, and some of the remainder were easily taught to do it also; a circumstance that was later of great assistance in judging whether, or no, the recovery of coördinated voluntary control of the muscles concerned in that movement had occurred. Other methods of testing, such as running up a flight of steps, holding a bone after the bandaging of the uninjured foot, etc., were also used. For the electrical investigation, a du Bois induction coil by Reininger, Gebbert, and Schall was employed. The primary circuit of the coil was attached to the mains of the 115-volt illuminating current with a sixteen candle-power lamp in series with the primary of the coil; .5 ampere of current was registered by the ammeter when the hammer was in action. During the electrical examination, insulating rubber was placed under the nerves to prevent the escape of current to neighboring nerves.

After the animals had been killed, very careful dissections of the united nerves were made. In the animals referred to in this paper it was found, unless it is specially mentioned to the contrary, that the crossed nerves had united in the position in which they had been sutured, and that they were not united in a common cicatrix. If the adjacent united nerves were at all firmly adherent, the result was considered questionable, and was thus rejected.

Experiments. — I. *Central portion of right ulnar sutured to the peripheral end of the right median; and the central median to the distal ulnar.*

Dog 1.— Operation January 8, 1895. Plaster bandage removed January 12, and wound found to be healing by first intention. On allowing the dog to run about, it did not appear to limp or seem much inconvenienced by the loss of the functional use of the flexors of the right foot and wrist. Careful comparison with the left foot plainly showed that the right wrist was considerably more extended than the left one, and when the dog was standing with this foot resting on the floor, a considerable part of the palmar surface of the metacarpus touched the floor. If both fore-legs were held up, movements of flexion and of extension of the left paw would occur, but the right paw was held in a state of moderate over-extension, the toes being slightly spread apart. When running up a flight of steps, the dog would often stumble, appearing to strike the edge of a step with the over-extended foot. Owing to the development of a few small ulcers on the plantar balls, the plaster bandage was again applied at

the end of a week, over the whole limb and shoulder, with a few turns around the body. In two weeks this plaster was removed, and on February 26 another careful examination of the animal was made. At this date, the over-extension continued. The right forearm was much smaller than the left from atrophy of the flexor muscles. On putting the left paw into a small boot and giving the dog a bone, the bone frequently slipped from under the right paw by which the dog tried to steady it when he attempted to gnaw it. No movements of the flexor muscles could be detected. After anæsthetizing the animal and exposing the crossed nerves, it was found that the central median had apparently united to the distal ulnar as well as could be desired. The bulbous ends of the crossed central ulnar and distal median had separated about three millimetres, but were connected by a delicate grayish thread-like band that was found to consist of new nerve fibres.

Faradic stimulation of the central median above the point of union produced movements in many of the partially exposed muscles innervated by the ulnar, causing ulnar flexion of the wrist and foot. Stimulation of the distal united ulnar three-quarters of an inch below the point of union also produced ulnar flexion, but not until the strength of the current had been considerably increased. Stimulation of the central ulnar with a rather strong current (10 cm.) produced a faint median flexion of the paw. The distal median had not recovered its faradic electrical irritability, and the electrical irritability of the right distal ulnar was much less than that of the left uninjured ulnar.

After exposing the sigmoid gyrus of both cerebral hemispheres, the areas for extension and for flexion of the paw were stimulated after the paw had been flexed and the arm and forearm made immovable by firm fixation; — extension of the paw readily followed the cerebral stimulus. Only a very slight degree of flexion of the paw could be produced by stimulating the fore limb area in the left hemisphere of this dog, although a stimulus sufficiently strong to produce a severe general fit was finally applied. The central ulnar and the central median nerves were then divided above the points of union and stimulated, the results being the same as before their division. The distal median was then divided and the central ulnar stimulated with a strong current; no flexion of the paw was produced. Stimulation of the central median readily produced ulnar flexion.

Dog 2.—Similar to No. 1, but the dog was kept for seventy-five

days. Over-extension of the paw was still present, and the animal was awkward and stumbled when running up the steps. Cutaneous faradic stimulation of the flexors of the paw showed that, although the faradic irritability of those muscles had been nearly recovered, their irritability was less than that of the flexor muscles of the normal left forearm. Faradic stimulation of the exposed united nerves showed that the nerves were irritable both above and below the points of union, and stimulation of the central ulnar produced well-marked contraction of the muscles innervated by the median. Excitation of the central median produced contraction of muscles supplied by the peripheral ulnar which had been crossed with it. Stimulation of the cortical area for flexion of the paw readily produced that movement.

Dog 3.—The right fore limb of this dog was kept for seven weeks in plaster. At the end of fourteen months, a moderate predominance of the extensors over the flexors of the paw was still evident when the animal was carefully examined. The dog also frequently stumbled when attempting to run rapidly up the steps, and though flexor movements of the right paw were plainly to be seen, the movements did not appear to be quite so actively made in the right leg as in the normal left one. Even after this interval of time, the toes of the right foot were still considerably separated when the animal was resting upon that foot. Electrical excitation of the flexor area of the cortex and of the exposed crossed nerves gave results similar to those met with in dog 2, and needs no further comment. The previously atrophied right flexor muscles had evidently nearly completely regenerated, for the forearms of the dog did not perceptibly differ in size nor did the quantitative faradic electrical irritability of the flexor muscles of the forearms differ much.

The preceding results thus corroborate those of previous workers, in that they clearly prove that one mixed nerve may be crossed with and unite with another mixed nerve. They also clearly demonstrate that the peripheral portion of the crossed united nerve recovers its function of conductivity before it recovers the property of electrical irritability. After the nerves have united and the various groups of muscles have regenerated, nervous impulses emanating from the motor cortex of the brain are still capable of causing the cells of the spinal cord from which the central portions of the crossed nerves arise, to discharge impulses that give rise to contractions of the muscles which the crossed nerves supply. But in the dog, as is well

known, the main functional use of the groups of muscles that are supplied by the ulnar and the median nerves is to produce flexion of the foot, the action of the groups of muscles being synergic and also usually synchronous. Consequently, very little, if any, disturbance of voluntary coördinated flexion of the paw would be likely to follow in the dog when the ulnar and the median nerves have been successfully crossed, a conclusion that is fully exemplified by the result obtained in dog No. 3.

II. *Central end of the right musculo-spiral nerve crossed with the distal portions of the ulnar and the median, and* vice versa.

This operation was performed on nine dogs, but in only four dogs were the experiments successful. In one of these four dogs, No. 2, a large, powerful, restless animal, so much swelling and induration of the tissues developed on the dorsal surface of the wrist from constant attempts to walk upon this surface, that it was impossible to definitely judge whether or not the dog was able to voluntarily contract the extensor muscles of the paw. Evidently the animal was not able to extend the paw intentionally, else it would not have continually flexed the foot at each step and come down upon the dorsal surface of the wrist and foot. Subsequent electrical investigation of the nerves and of the cortical centres showed, however, that the crossed nerves had become at least partially united and regenerated, and that they had recovered their conductivity and electrical irritability.

As the experiments on dogs 1, 3, and 4 yielded essentially uniform results, a description of the results obtained in dog 3 will thus apply to dogs 1 and 4.

Dog 3. — Nerves crossed January 20, 1895, and plaster bandage kept on for two weeks. Wound healed by first intention. Plaster reapplied and kept on for four weeks. Muscles of right forearm markedly atrophied and did not respond to cutaneous faradism. In the course of a week, some contraction of the flexors of the paw, which did not fully relax when elbow was extended. The dog continually held the forearm flexed and the foot was not allowed to touch the ground. When given a bone the animal would attempt to steady it in order to gnaw it by resting the outer side of forearm and flexed foot upon the bone, but was not very successful in keeping it firm.

On October 11th, the dog attempted to use the right leg for walking, but whenever he did so, walked on the back of the foot, on the outer

surface of which was a small ulcer. Ether was administered, the crossed nerves exposed, stimulated, and found to have united. Their electrical irritability had been recovered. Many of the flexor and extensor muscles also responded to direct faradization. After closing the wound and applying an antiseptic dressing to it, and also to the ulcer on the foot, the whole limb was put in plaster with the foot extended. At the end of three weeks the plaster was removed, and the wound and the ulcer were found to be healed. From that time until June 29, 1896, the dog was frequently examined, and the muscles stimulated with mild faradic currents, after previously muzzling the dog, which submitted to this treatment without any especial resistance.

On June 29, 1896, the forearms scarcely differed in size. The muscles of the right forearm seemed to be almost completely regenerated. The right paw was held partially flexed, but when it was carefully observed after steadying the forearm at the elbow, alternating movements of flexion or extension of that paw could be readily seen to occur. When the dog was ordered to give this paw, the animal lifted up the forearm, but instead of extending the foot, the latter was very visibly flexed. Every time the dog walked, the right leg was advanced but the paw was quickly flexed. When a bone was given to the dog, after inserting the left foot in a boot and immobilizing the left wrist by means of a small splint, the movement of the muscles of the right forearm appeared to be so extremely incoördinated that the animal finally held the bone by resting the middle of the forearm upon it. Irregular movements of the adductors and abductors of the toes were also noticed. It should be remarked that this dog had exhibited the above movements early in February, 1896, but certainly no improvement in the coördination of the movements had occurred when the above final examination was made.

The dog also seemed to have recovered sensation on all surfaces of the foot, but the various tests with clips, etc., for determining whether, or not, the animal could correctly localize the position of the peripheral stimulus gave such conflicting results that I am not able to give an opinion in regard to this subject. After anæsthetizing the animal, exposing the motor cortex of both hemispheres, and firmly fixing both elbows so as to prevent any movement at the elbow joint, the cortical area of the right hemisphere for flexion of the wrist was stimulated with a minimal current, and then the same strength of stimulus applied to the area for flexion in the left hemisphere. Result: Extension of the right wrist. Stimulation of the

extensor area, a little further forward in the sigmoid gyrus, produced flexion of the left paw. After repeating this several times the musculo-cutaneous nerve was divided, together with the various flexors and extensors of the forearm; the crossed nerves and blood-vessels being carefully dissected away and protected by cotton wet with warm normal saline solution. After firmly fixing the elbow, the cortex was again stimulated; the flexor area giving rise to contraction of the extensor muscles, the extensor area to flexion of the paw, accompanied apparently by extension of the first phalanges when the current was slightly strengthened.

Two minims of the French oil of absinthe were then injected into the jugular vein. In a few minutes the usual absinthe fit occurred. During the tonic fits the left foot was extended and the right flexed. On immediately excising the small area (extensor) of the left hemisphere, which had been electrically determined to produce flexion of the right foot, the right foot became extended. During another fit the flexor area was excised and the exposed extensor muscles of the right foot no longer participated in the fit.

The preceding results thus conclusively show that the spinal nerve cells from which the musculo-spiral and the ulnar and median motor fibres arise still preserve their connections with the cortical motor mechanisms situated in the sigmoid gyrus.

As far as the cortical areas of this region are concerned, there does not seem to be the least ground for stating that these centres readjust themselves to suit the altered innervation of the groups of muscles which the two united crossed nerves supply. Nor did five months' practice seem to enable the adult dog to regain the functional use of the muscles of the forearm and foot, for, as I have previously remarked, very evident and ample volitional, but incoördinated, movements were visible about five months before the dogs were killed, and none of the dogs showed the least improvement in acquiring any better control of the muscles supplied by the crossed nerves.

III. *Will the rhythmic contractions of certain groups of muscles reappear after union of their motor nerve with the central end of a motor nerve to non-rhythmic muscles?*

To investigate this question, the right recurrens was divided in three dogs as low down in the neck as possible. After carefully freeing the long peripheral portion of the recurrens, it was turned upward around the border of the inferior constrictor of the pharynx and sutured to the

central end of the hypoglossal, which had been cut close to the tongue. The central end of the recurrens was ligated with fine silk, turned toward the root of the neck, and sutured with catgut to the adjacent tissue. Before this operation, these dogs barked very frequently, but after the operation the animals were only able to utter an imperfect, hoarse, stridulous growl. The right half of the tongue was paralyzed, and soon became atrophied and fissured. At the expiration of eight months, it was noticed that the atrophic condition of the right half of the tongue was beginning to lessen, except in dog 3, and also that two of the dogs could move the muscles of that half considerably. At this date, when examined under ether, the regenerated muscles of the right half of the tongue readily responded to faradism. At the end of fourteen to fifteen months, the movements of the tongue seemed to be almost completely restored, except in dog 3, in which the right half of the tongue was permanently paralyzed. Fourteen to fifteen months after the primary operation, the dogs were etherized and the trachea divided just below the larynx. After the insertion of a tube with a short rubber pipe attached to facilitate the administration of the anæsthetic, the anterior composite convolution of both hemispheres was exposed and stimulated with an electrode, the points of which were set one millimetre apart. By carefully adjusting the narcosis, using a stimulus just strong enough to cause the vocal cord to nearly approach the middle line, and carefully removing fluid on the convolutions before applying the electrodes, it was perfectly possible to obtain from both hemispheres adduction of the left vocal cord without any accompanying movements of the tongue when the junction of the præcrucial gyrus and the upper extremity of the anterior composite was stimulated.

When carefully observed[1] from below, or from above, through the widely opened mouth, the right vocal cord was seen to be perfectly immovable. In all of the dogs its position seemed to be about midway between adduction and abduction. When the central hypoglossal or the recurrens which had become grafted to it were stimulated, very evident movements of adduction or of abduction would occur. Sometimes the cord would begin to abduct and then suddenly adduct. When the above-mentioned focus in either hemisphere was stimulated, no movement of the right vocal cord followed unless a very strong

[1] In this connection, the writer wishes to thank Professor Frederic S. Lee for his kindness in carefully observing the movements of the vocal cords on various occasions.

current (secondary at 4 cm.) was applied. With this strong stimulus, movements of the tongue and of swallowing also occurred. Minimal stimulation of the left anterior composite gyrus farther back, where it is joined by the supra-sylvian, was followed by bilateral movements of the split tongue, with adduction, or frequently with abduction, of the right vocal cord. The rhythmical movements of the left were not interrupted. Stimulation of the corresponding area of the right hemisphere produced bilateral movements of the tongue with moderate abduction of the right cord. The left cord did not respond. With the coil at 3 cm., adduction of the right cord occurred.

The left recurrens was then divided, in order to stop the respiratory movements of the left cord, and the above-mentioned regions again stimulated. The movements of the right cord accompanying the movements of the tongue were then more striking, but stimulation of the hemispheres at Krause's laryngeal centre did not produce a movement of the right cord, unless, as previously stated, a current sufficiently strong to produce violent efforts of swallowing was employed.

After killing the dog with the anæsthetic, a dissection of the united nerves disclosed the fact that not only had the sutured recurrens united to the central hypoglossal but that from the latter numerous outgrowths had grown to the base of the tongue and had evidently united with the old peripheral hypoglossal stump. The regeneration of the tongue muscles and the return of voluntary control of the tongue was thus readily explained.

A search for the central end of the right recurrens disclosed the small knobbed end of this nerve about in the position in which it had been sutured; it seemed to be attached to the sterno-thyroid muscle. It had clearly not re-established any connection with the laryngeal muscles.

In dog 3, in which the sutured nerves had been rolled up in a piece of fascia, the outgrowths of nerve fibres from the large hypoglossus had not succeeded in reaching the tongue and producing regeneration of its muscles. When the cortex of this dog was stimulated, no movements appeared in the right half of the split tongue. The right vocal cord responded as in dogs 1 and 2, and no respiratory vocal cord movements could be detected after the section of the left recurrens.

Evidently, therefore, the cells of origin of the hypoglossal nerve do not assume the rhythmical functions of the cells of origin of the recurrens when the latter nerve is made to unite to the central portion of

the former. Clearly, the nerve impulses proceeding from certain nerve centres that innervate the muscles supplied by the recurrens do not shunt off by new or by old paths to the hypoglossal nucleus, when this nucleus, or a part of it at least, is caused to become the nucleus of the recurrens. How much the less likely, therefore, that the hypoglossal nucleus should assume all the functions of the nucleus of the vagus, were that nerve united to the hypoglossus.

To conclude, it is evident that in the dog the central portion of one motor nerve may unite with the peripheral portion of another motor nerve; that the cortical representation of the groups of regenerated muscles supplied by the crossed and united distal nerve is the same as the cortical representation of the groups of muscles that were previously innervated by the central portion before its section; that this cortical representation of the groups, after crossing the nerves, differs from that existing before the nerves are crossed, in that the cortical impulses produce incoördinate movements of the muscles supplied by the united crossed nerve. If two motor nerves supplying two groups of synergic muscles, whose action is to produce almost similar simple movements of an articulation, be crossed, the resultant disturbance of the coördinated mobility of those synergic groups is exceedingly slight, as regards the performance of that particular movement. When groups of muscles innervated by the crossed nerves are of widely different functional use, antagonists, etc., the adult animal (dog) does not regain the power of performing intentional coördinated movements with those muscles, although the fibres of the muscles completely regenerate and recover their former irritability.

Crossing the peripheral portion of the motor nerve of rhythmically contracting muscles to the central portion of the motor nerve of non-rhythmic muscles results in the permanent abolition of the rhythmic action of the former muscles.

In view, therefore, of the foregoing results, it is evident that the central nervous mechanisms do not, as Rawa has claimed, adjust their impulses to suit the altered peripheral innervation, and, by practice, supply exactly what is required of them by the peripheral organs with which they become connected.

From the Physiological Department of Columbia University, New York.

[*Reprinted from the Journal of Physiology. Vol. XXII. No.* 4, *February,* 1898.]

THE CORTICAL MOTOR CENTRES OF THE OPOSSUM, DIDELPHYS VIRGINIANA.

By R. H. CUNNINGHAM, M.D., *Demonstrator and Alumni Fellow in Physiology, Columbia University, New York.* (One Figure in Text.)

Although the cortical motor centres of many of the lower mammalia and of various birds have been carefully investigated and more or less accurately mapped out by a number of observers, chief among whom are Ferrier, Obersteiner, Albertoni and Michieli, Fuerstner, Mann, and Mills, there seems to exist, so far as I can discover, no description[1] of the various cortical motor centres that are found in the brain of the opossum. To be sure, the microscopical as well as the macroscopical anatomy of the opossum brain has been minutely described by Herrick[2], who regards the precrucial lobe as typically motor in its microscopical structure and the parietal and occipital portions of the cortex as composed of motor and other nerve cells, but this writer does not state whether or no these views have been corroborated by a physiological investigation of the cortex with the electric current. Hence the experiments described in this paper were made with the view of accurately determining what portions of the cortex of the opossum are electrically excitable. The surface anatomy of the pallium of the opossum resembles very much that of the hedgehog, whose cortical centres have been described in detail by Mann[3].

On the pallium of the opossum the transverse sulcus, or *præsylvian* fissure as it is termed in the hedgehog brain by Mann, is usually well defined and situated at the junction of the anterior and

[1] Since this paper was forwarded to the editor I have found in the *Centralblatt für Physiologie*, Oct. 16, 1897, that Professor Ziehen has recently investigated the location of the cortical motor centres in one young, slightly etherized opossum. His results differ so from mine that I can venture no other explanation than the one fully discussed in this paper, namely, the employment of a very strong electrical stimulus (secondary coil at one centimetre from the primary being necessary to excite the fore limb centre) on an incompletely anæsthetized animal.

[2] C. L. Herrick. *Journ. of Compar. Neurology*, II. p. 1. 1892.

[3] Mann. *Journ. of Anat. and Physiol.* XXX. p. 1. 1895.

second fourths of the cranial surface of the pallium. The dorsal cortex is thus separated into a small so-called precrucial portion and a large parieto-occipital portion. Laterally, each hemisphere is separated into a dorsal and a ventral portion by the rhinal fissure. The sylvian fissure is inconspicuous and does not extend across the rhinal fissure. The olfactory lobes are very prominent and are larger in the opossum in proportion to the cerebrum than is the case in the hedgehog; but in other respects the superficial configuration of the brain of the marsupial opossum is, as has already been stated, practically identical with that of the hedgehog.

Experiments.—Of the three opossums employed for this investigation one was a young male, the others elderly females. Ether narcosis was induced in all the animals and great care was exercised to maintain a proper degree of anæsthesia during the entire experiment; for, according to the experience of the writer, in order to obtain results with any pretensions to accuracy it is absolutely essential for the animal not to be imperfectly anæsthetized. Early in each experiment tracheotomy was performed and a large cannula inserted. To the cannula a rubber tube was attached and the administration of the ether conducted through the tube during the rest of the experiment. By so doing danger of possible local action of the escaping ether vapour on the cortex was considerably diminished. After rapid exposure of a large portion of one hemisphere and the anterior region of the other and the checking of all hæmorrhage from the bone by means of plastic wax, the cortex was covered with a small pad of cotton well moistened with warm normal saline solution. The skin flaps were then replaced and all further manipulations except the etherization suspended for about fifteen minutes in order to allow the brain to recover from the shock. Then the warm cotton was removed, and all adherent fluid was gently mopped up from the surface of the brain; next, the stimulator with its platinum-pointed electrodes 1 to 2 mm. apart was systematically applied for about five seconds to certain regions of the cortex and the results carefully noted[1]. After several adjacent areas had been explored with induced currents of different intensities, the warm cotton was replaced and the cortex allowed to rest for five or six minutes before the electrodes were reapplied to other regions of the cortex. After the position of the various centres had been determined

[1] In this connection the writer wishes gratefully to acknowledge his indebtedness to Dr Reid Hunt, for his kind and careful assistance rendered during this stage of the experiments.

and repeatedly verified, their distance from two fixed points was measured and their location marked upon an accurate diagram of the brain drawn to scale upon paper ruled in small squares. Finally each animal was killed with an overdose of ether and its brain removed, photographed, and preserved for future reference.

Exp. 1.—Female opossum. Left hemisphere first exposed and stimulated, later the right hemisphere and a large part of the olfactory lobes were also explored. Distance between electrodes = 1 mm. Unless otherwise noted, the movements occurred on the side of the body opposite to that stimulated. Stimulation of the centres 1—7 (Fig. 1) gave rise to the following movements:

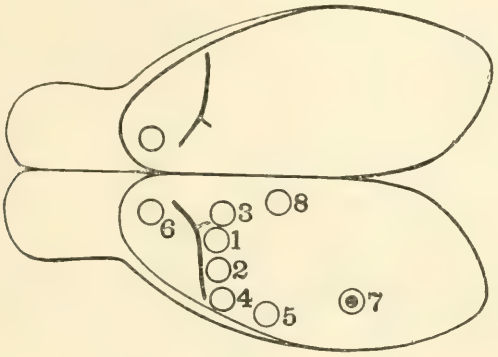


Fig. 1.

(1) Extension of digits of fore-paw and of the wrist. Toes widely separated. With a current of less intensity extension with adduction of the first toe frequently took place. With a very weak current extension of the first toe alone was produced.

(2) Flexion and adduction of the toes. Flexion of the wrist. These movements could only be elicited during the earlier stages of the experiment.

(3) Elevation of the shoulder, advancement forward of the arm, partial flexion of the forearm, extension of the wrist and digits.

(4) Bilateral facial movements. Momentary elevation of left lip and twitching of eyelids. Respiration much slowed. On holding the mouth open a very distinct tremor of the tongue was visible when the stimulus was acting.

(5) Opening of the mouth, movements of the tongue, and often the act of deglutition followed.

(6) A slight twitching of the alæ of the nose occurred with a strong current; nothing with a weak one. Application of the same current to the olfactory lobes produced the same result. Stimulation of the precrucial regions of both hemispheres at the same time gave rise only to a more marked twitching of the nares. Application of a very strong current (secondary coil of the du Bois inductorium at 4 cm.) to one precrucial lobe for five seconds gave rise to a slight general fit, which apparently began in the shoulder and fore-limb.

(7) Opposite ear drawn backward and its extreme tip folded inward.

Stimulation of the occipital and other portions of the cortex were without results.

Exp. 2.—Young male opossum. The results obtained in this animal were practically the same as in the preceding experiment except that the movements described under (2), and the infolding of the tip of the ear could not be produced by stimulating the cortex. At the point designated by (8) on the diagram, the application of the electrodes was in one instance followed by the drawing up of the opposite hind-limb and immediately afterward by slight, apparently voluntary movements of the other limbs; but after regulation of the anæsthesia and repeated reapplication of the electrodes to this point as well as to various other spots in its vicinity, no discernible response could be detected in the hind-limb.

Exp. 3.—Elderly female opossum. The infolding of the tip of the opposite ear could not be produced; the location of the centre (7) was slightly different from that in Exp. 1, being situated two millimetres further forward. Otherwise the results in this animal were the same as those in Exp. 1.

After an examination of the above results it seems rather remarkable that in none of the opossums could trustworthy movements of the hind-limb be produced by stimulating the cortex, for one would suppose that the hind-limb movements ought to be fairly well represented in the cortex, since the hind-paw of the opossum is furnished with a peculiar thumb-like toe which the animal skilfully uses like a thumb in climbing or moving about in small trees. Nevertheless when I recalled to mind the results of several stimulation experiments performed by me several years ago on the brains of rabbits and other rodents, this apparent absence of cortical representation for movements of the hind-limb in the properly anæsthetized opossum is exactly what

I thought would probably be found. Like Mills[1] and certain other investigators I have never been able to produce in properly anæsthetized rabbits and other smaller rodents definite movements of the hind-limb by stimulating the cortex with a current of reasonable intensity. If the animal be first deeply etherized, as is usually done while the cranial cavity is being opened, and then the etherization suspended for the profound narcosis to diminish, it generally happens that just before the animal recovers sufficiently to make more or less haphazard voluntary movements of the limbs and body, it falls into a peculiar quiet state in which it seems to be very profoundly narcotized. In reality, however, the narcosis is slight, and the application of even a mild electrical stimulus to the cortex will often so arouse the animal that it will suddenly make fairly vigorous struggling movements. Thus, in the earlier stages of this imperfect, lessening narcosis even mild electrical stimuli, momentarily applied to the so-called cortical hind-limb centres of the rodent brain, will usually be productive of more or less brief movements of the opposite hind-limb which are by no means always uniform even though the electrodes be applied each time to the same region of the cortex. With a stimulus applied for five seconds both hind-limbs and even both fore-limbs often move. Such general movements may either quickly subside or continue until the animal is quieted by a further dose of the anæsthetic. Evidently, under the former circumstances, the cortical stimulation arouses the depressed animal just enough for it to make a few brief, voluntary struggles, and in the latter case the narcosis is sufficiently slight for the stimulus to arouse the animal completely.

As regards the cortical representation of the movements of the hind-limb my experience in the opossum was similar to the one above described in rodents. Only in a condition of imperfect narcosis was it possible to produce by stimuli of reasonable strength movements of the opposite hind-limb. Therefore, it was impossible to definitely locate a centre, or centres for movements of the hind-limb in the cortex of the above-mentioned opossums. A careful search for a centre controlling the movements of the prehensile tail also resulted negatively. Stimulation of the occipital region did not produce movements of the eyes.

The cortical representation of the fore-limb, of the mouth and tongue, of the muscles of deglutition and of those causing movements

[1] Wesley Mills. "Cortical Cerebral Localization, etc.," *Trans. of the Royal Soc. of Canada*, II. 1896-97.

of the ear seems to be well marked, although from my results it can not be said that the foci for the individual movements executed in those regions of the body are sharply differentiated. Lastly, if one compares the preceding results with the fairly elaborate ones obtained by Mann in the hedgehog, it is evident that the locations of the various excitable cortical centres are slightly different in the two animals, and that although the general configuration of the dorsal cortex of the opossum very much resembles that of the hedgehog, one must conclude that the cortical centres of the marsupial opossum are on the whole not so well organized as those of the insectivorous hedgehog.

Nov. 1897.

Studies from the Department of Physiology of Columbia University, at the College of Physicians and Surgeons, New York. Vol. I.

[*Reprinted from the Journal of Physiology. Vol. XXII. No. 3, November* 20, 1897.]

ON THE PATHS OF ABSORPTION FROM THE PERITONEAL CAVITY.

By S. J. MELTZER, M.D., New York.

The new theory that absorption of fluids from the peritoneal cavity is accomplished chiefly by the blood vessels, *i.e.* the fluid enters into the blood directly through the walls of the blood vessels, was brought about by the following three different sets of experiments conducted independently by different investigators. Starling and Tubby[1] found that coloured fluid introduced into the peritoneal cavity appeared first in the urine before it presented itself in the lymph flowing from the thoracic duct. Heidenhain[2] and Orlow[3] have established the fact that during the process of absorption of salt solutions from the abdominal cavity there is no increase in the flow of the lymph. Hamburger[4] finally reported that ligature of the innominate vein in rabbits (ligature of thoracic duct) does not influence the rate of absorption from the peritoneal cavity.

In an article on this subject, however, by I. Adler and the writer[5] it was conclusively demonstrated that neither the method which Hamburger employed nor his facts justify his positive conclusions. The rate of absorption varies too much in different rabbits to permit any comparison of rates under different conditions. With regard to the experiments of Heidenhain and Orlow we argued that though the facts in their experiments are unassailable the authors have not proved, and did not even attempt to prove, that the fluid which disappeared from the abdominal cavity actually entered into the blood. We have taken the ground that the salt solution which disappears from the

[1] Starling and Tubby. This *Journal*, XVI. p. 140. 1894.
[2] Heidenhain. *Pflüger's Archiv*, LXII. p. 320. 1895.
[3] Orlow. *Pflüger's Archiv*, LIX. p. 170. 1895.
[4] Hamburger. *Archiv f. (Anat. u.) Physiol.*, 1895, p. 281.
[5] I. Adler and S. J. Meltzer, *Journal of Experimental Medicine*, I. p. 482. 1896.

peritoneal cavity of living and dead animals does not enter into the blood vessels but remains in the interstitial spaces of the surrounding tissue, and its primary effect upon the blood is to reduce correspondingly the exudation of an isotonic fluid from the blood into the so-called lymph spaces. Without entering here any further into a detailed discussion of these arguments, I will only say that the experiments of Heidenhain and Orlow also do not prove that where absorbed substances actually enter into the circulation, they enter preferably through the walls of the blood vessels.

Having thus disposed of two of the sets of experiments my attention was now turned to the third set, to the experiments of Starling and Tubby, which, if confirmed, would indeed prove the correctness of the blood-vessel theory of absorption. A short analysis of their work will, however, reveal some inconsistencies; and these led me to test their statements in a series of experiments. Starling and Tubby have studied the subject under the head of absorption from serous cavities, investigating the absorption from the peritoneal as well as from the pleural cavity. Altogether they made twelve experiments, nine on the pleura and three on the peritoneum, and they sum up the results for both cavities together. In all cases, they say, the urine became coloured before the lymph. Five to twenty minutes after the injection of the coloured fluid into the serous cavities the urine was as coloured as the injected fluid, while it took ten minutes to four hours before the lymph became slightly tinged with the colour. The authors arrive at the somewhat radical conclusion that it is even very doubtful "whether the slight colouration of the lymph which was observed in these experiments is occasioned at all by lymphatic absorption." If methylene blue or indigo-carmine, they say, be injected into the bloodstream, the lymph flowing from the thoracic duct within half a minute becomes coloured. (They do not tell us how soon under these circumstances the colour appears in the urine.) The writers therefore suppose that the colour of the lymph in their experiments may have been "caused by passage of coloured lymph from the blood vessels, not by any direct absorption of the blue from the serous cavity." It seemed to me that their additional experiment on the injection into the bloodstream is not of a nature to strengthen their somewhat radical position. The coloured substance which leaves the blood to appear in the lymph enters first into the "lymph spaces"; so does that which is absorbed from the peritoneal cavity. Now while in the former case it takes the coloured substance less than half a minute to travel from the lymph

spaces to the thoracic duct, the coloured substance in the lymph spaces adjacent to the serous cavity does not in some cases, according to Starling and Tubby, reach the thoracic duct before four hours, and possibly never reaches it at all in the straight way of the lymphatic absorption. Furthermore, the writers were not fortunate in the selection of their illustrations. They publish two protocols, one from the experiments on the pleural and one from that on the peritoneal cavity. In experiment I., showing the absorption from the pleural cavity, the rate of the lymph flow before and shortly after the introduction of the coloured fluid into the pleura was 0·04 c.c. per minute. In all the numerous protocols of Heidenhain and others as well as in my own observations on the lymph flow I have never met with such a low rate. Besides, in this experiment, there was, contrary to their own statement, a distinct increase of flow with the progress of absorption, which, by the way, was exceedingly small, less than 0·05 c.c. per minute. There was certainly some abnormal condition present in this experiment and it cannot be regarded as proof against the participation of the lymphatics in the absorption from the pleural cavity. In experiment II., illustrating the absorption from the peritoneal cavity, the absorbed amount is also surprisingly small. During two hours and twenty minutes not more than 25 c.c. of the isotonic fluid were absorbed from the peritoneal cavity of a dog weighing about 5 kilos, making about 5 c.c. pro kilo. In the experiments of Orlow and of Heidenhain we find that the amount of isotonic fluid absorbed in about an equal period was never less than 10 c.c. pro kilo.

The series of experiments of which I give an account here are in substance a simple repetition of those made by Starling and Tubby. I have confined myself, however, to the question of absorption from the peritoneal cavity[1].

The method was in the main the same as that employed by the authors mentioned; *i.e.* coloured fluid was introduced into the peritoneal cavity and the first appearance of the colour in the lymph and the

[1] Incidentally I wish to remark that the factors controlling absorption differ so widely in the pleural and the peritoneal cavity that it is by no means justifiable to put them together under the one head of serous cavities and implicitly to draw conclusions as to one cavity from experiments made on the other. It will suffice to point out two such factors. 1. Recklinghausen, who established the great absorbing capacity of the peritoneal surface of the diaphragm for fluids containing corpuscular elements, found that the pleural surface did not absorb. 2. The presence of the respiratory mechanism in the pleural cavity with the rhythmical changes between suction and pressure which surely exerts a special influence upon the process of absorption.

urine noted. A glass cannula, bent to a right angle, was tied in the left thoracic duct of a dog, in the usual manner. The right lymphatic duct was left untouched. With regard to the collecting of the urine, the method differed somewhat from that employed by Starling and Tubby. These authors described their method in the following way. "A cannula was tied into the ureter, or in most cases into the bladder, either through an opening in the abdominal wall or through an opening in the urethra, which was exposed by splitting the symphysis pubis." For reasons which I will touch upon later I avoided any method which implies the opening of the abdominal cavity or splitting the symphysis; I therefore preferred to introduce a catheter into the bladder through an external opening in the urethra. In female dogs this is quite a simple procedure. The catheter is introduced through the external meatus of the urethra which becomes plainly visible as soon as the posterior wall of the vestibule is split. In the male dog the catheter has to be introduced through an opening made by external urethrotomy which is by no means an easy task. I may also especially mention that after the introduction of the coloured fluid into the abdominal cavity the opening was carefully stitched and clamped and special pains were taken to prevent the entrance of the fluid into the space between the muscles and the skin. The animals were always anæsthetized, mostly in the manner used by Starling and Tubby, *i.e.* first by a hypodermic injection of morphine and then by inhalation of a mixture of A.C.E. (alcohol, chloroform, ether). The protocols of these experiments will speak for themselves.

Exp. 1. Male dog, 22 kilograms. At 5.20 p.m. injected about 76 c.c. of 1 % indigo-carmine. Wound thoroughly cleansed and clamped. Respiration and pulse continually good. Lymph flow fair, collected in a test tube. At 5.34 lymph distinctly blue. Urine continues to be normal in colour until 6.40 when the first greenish tinge appears, at 6.45 urine perfectly dark. Animal killed. The entire amount of lymph 15 c.c., average about 0·2 c.c. per minute, continued to be blue to the end. The colour appeared in the lymph fourteen minutes, in the urine eighty minutes after the injection of the indigo-carmine into the peritoneal cavity.

Exp. 2. Male dog, 26 kilos. At 5.29 p.m. injected into peritoneal cavity 50 c.c. of methylene blue (1 %). Lymph greenish blue at 5.55 p.m. Urine shows tinge first at 6.49 p.m. Flow of lymph never less than 0·4 c.c. per minute. Colour appeared in lymph twenty-six minutes, in urine eighty minutes after the injection of the methylene blue into the abdominal cavity.

Exp. 3. Male dog, 21 kilos (anæsthesia by ether, tracheotomy, now and then, for a minute or two, artificial respiration). At 4.50 introduced into the abdominal cavity 40 c.c. of potassium ferrocyanide (10 %), the presence of this salt in the lymph or the urine tested by perchloride of iron either on a small piece of absorbent cotton or in a test tube. At 5.4 the reaction of Prussian blue appeared in the lymph, the first faint reaction in the urine appeared at 5.45 and did not become distinct until ten minutes later. The urine was scanty. The reaction of Prussian blue appeared in the lymph fourteen minutes and in the urine fifty-five minutes after the injection of potassium ferrocyanide into the abdominal cavity.

Exp. 4. Male dog, 30 kilos. At 5.27 p.m. injected 50 c.c. indigo-carmine (1 %) into the peritoneal cavity. Lymph distinctly coloured at 5.40, urine tinged at 6.11 and quite dark at 6.15. Thirteen minutes for lymph and forty-four minutes for urine.

Exp. 5. Female dog, 18 kilos. At 5.43 injected into abdominal cavity 50 c.c. indigo-carmine (1 %). Lymph reddish, clots readily and flows quite slowly. At 5.55 lymph tinges blue. The colour remained during the entire experiment quite faint. The urine becomes blue at 6.23. Twelve minutes for the lymph and forty for the urine.

Exp. 6. Female dog, 28 kilos. At 4.15 p.m. introduced into the abdominal cavity 50 c.c. indigo-carmine (1 %). Lymph thin, hardly clots, flows freely. At 4.23 lymph distinctly blue, the urine becomes coloured at 4.41. Lymph after eight and urine after twenty-six minutes.

Exp. 7. Male dog, amount of lymph in five minutes measured throughout entire experiment. At 5.30 injected 500 c.c. of salt solution (0·2 %) containing five grams of indigo-carmine. Blue colour appeared in the lymph at 5.41 and in the urine at 5.53—eleven minutes for the lymph, and twenty-three minutes for the urine. The rate of flow of the lymph in the thirteen minutes before the introduction of the fluid into the abdomen was reduced from 1 c.c. p.m. in the beginning to 0·52 c.c. p.m. After injection it gradually increased to 1·18 c.c. until 5.46 p.m. when it decreased again gradually to 0·7 c.c. p.m.

Exp. 8. Female dog, 12 kilos. At 4.28 injected into abdominal cavity 4 c.c. of salt solution (0·5 %) plus 2 c.c. methylene blue (1 %) and at 5.6, 500 c.c. of salt solution (0·2 %) was again introduced into the peritoneal cavity. At 4.44 the lymph appeared greenish blue. The urine though flowing liberally did not show any trace of the colour up to 6.0 p.m. when the experiment had to be discontinued. In this experiment, too, the lymph was measured every five minutes throughout the entire experiment. It started with 0·48 c.c. and came down to 0·28 c.c. p.m. shortly before the first injection. Then it varied irregularly between 0·21 and 0·34 c.c. per minute throughout the rest of the experiment.

Exp. 9. Male dog, 10 kilos. At 4.30 injected into the peritoneal cavity 50 c.c. of indigo-carmine (1 %). Flow of lymph good, lymph bluish at 4.43, urine blue at 4.53—thirteen minutes for lymph and twenty-three minutes for urine.

Exp. 10. Male dog, 30 kilos (anæsthesia by ether). At 5.36 injected into abdominal cavity 80 c.c. of potassium ferrocyanide (12 %). Lymph shows reaction of Prussian blue at 6.11, urine shows no trace at 6.35 when experiment had to be discontinued.

In all these ten experiments, the coloured fluid or the characteristic reaction of Prussian blue appeared invariably in the lymph distinctly earlier than in the urine—the reverse of the result obtained by Starling and Tubby. I possess protocols of a few more experiments which I abstain from recording here as they do not bring out any important new points, but in which again the colour or the reaction (of salicylate of sodium) appeared first in the lymph and later in the urine. The lapse of time between the injection into the abdomen and the appearance in the lymph was in all the experiments approximately the same—an average of fifteen minutes. Of course, the rate of flow, the coagulability etc. had some influence upon the length of the interval, but they seemed to influence rather the intensity of the colour or reaction than the time of its first appearance in the lymph. On the other hand the time for the first appearance of the colour etc. in the urine varied considerably in different experiments. The rate of flow of the urine had hardly any distinct influence upon the time of the appearance of the colour in it. I shall not attempt to discuss here the possible causes which hastened or retarded the appearance of the colour in the urine. I wish only to add that, in the few experiments I made by injecting coloured fluid directly into the circulation, the colour appeared in the lymph before it appeared in the urine; the interval for the lymph was approximately constant, while the interval for the urine was quite variable—between seven and thirty-four minutes.

However, the determination of the intervals which elapse between the introduction of the substances into the peritoneal cavity and their appearance in the lymph and in the urine is of secondary importance, at least in our present discussion. The sole object of the series of experiments which I have reported here was to test the statement of Starling and Tubby that coloured fluids injected into the peritoneal cavity appear in the urine earlier than in the lymph. As I have said in all my experiments the colour or the characteristic reaction appeared in the lymph unmistakably earlier than in the urine. Starling and

Tubby have made three experiments on the peritoneal cavity[1], I made fourteen. It is hardly possible to give any decisive explanation of the differences of the results. It might be pointed out, however, that Starling and Tubby have apparently used very small dogs for their experiments, which could account in some degree for the delay of the substances in the lymph, as the lumen of the cannula which they had to employ must necessarily have been quite narrow, which would in itself be sufficient to retard the flow, but would the more do so by giving rise to the formation of a partial clot. I may remark that a partial clot may retard the flow without stopping it altogether. Experiment I. of Starling and Tubby seems to sustain this suggestion. As to the exceedingly early appearance of the colour in the urine in some of the experiments of Starling and Tubby I would recall that the method which they have employed permits a suspicion that some of the coloured fluid entered directly into the bladder or urethra. It seems that in closing the wound they have omitted to stitch and clamp the muscles of the abdomen, but had one limb of the cannula "fastened by ligatures round the skin of the wound." Such a method allows the fluid to escape from the abdominal cavity and pass between muscles and skin along the linea alba down to the symphysis which was split for the purpose of introducing a cannula into the bladder.

We have thus been able to refute the claims of the entire chain of experiments brought forward in favour of the theory that the peritoneal absorption takes place through the walls of the blood vessels and not by way of the lymphatics. We have shown that if the method employed in Hamburger's experiments permits any positive conclusion this would come out rather against than for the conclusion drawn by him.

Against the experiments of Starling and Tubby in favour of the blood-vessel theory we brought experiments showing results just exactly the reverse of theirs.

We have finally shown that the experiments of Heidenhain and Orlow, though true in their facts, do not permit any conclusions in favour of one or the other theory.

On the other hand, the experiments of Adler[2] and myself with strychnine and potassium ferrocyanide have shown that these substances

[1] For reasons I have stated above I do not believe that their experiments on the pleural cavity can be adduced as evidence for the conditions existing in the absorption from the peritoneal cavity.

[2] *loc. cit.*

under normal conditions are preferably absorbed by the lymphatics. But they have also shown that when the lymphatics are blocked, the substances mentioned can be taken up also by the blood vessels, though the absorption appears under these circumstances to be very much retarded. It must, however, be pointed out that in these experiments we only know of the absorption of these substances alone and not of the fluid medium in which they were dissolved, and we must also bear in mind that the substances which were employed in these experiments are normally foreign to the animal body. Of the fate of the solvent, however, we know as much as we know of that of the plain salt solutions which are brought into the peritoneal cavity without the admixture of a substance foreign to the animal body, *i.e.* we know very little. What we positively know is only that they disappear in the adjacent interstitial spaces but we have so far no experimental proof as to their further fate, and all that can be said about it as yet is mere hypothesis. I believe, however, that in the consideration of this question a certain progress is made by the introduction of the interstitial spaces as a first station in all cases of absorption of fluid from the peritoneal cavity and also as a final station for the absorption in dead animals.

PHYSIOLOGICAL EXPERIMENTS WITH

INTESTINAL IRRIGATION.

ON PULSE TENSION, TEMPERATURE, RENAL SECRETION, AND INTESTINAL ABSORPTION.

COMPARATIVE TABLE, WITH INFUSION, HYPODERMOCLYSIS, AND ENTEROCLYSIS, ON RENAL EXCRETION.

SOME FURTHER REMARKS ON IRRIGATION.

By Robert Coleman Kemp, M.D.

In the *New York Medical Journal,* March 13, 1897, there appeared an article by me entitled Indications for the Use of the Double-current Rectal Irrigator, Solutions Employed, Temperature of the Fluid, etc. Having noted clinically the diverse effects produced by the different temperatures, I determined to undertake a few physiological experiments as to the effect of continuous intestinal irrigation on the pulse tension, temperature of the body and blood, renal secretion, and intestinal absorption. These experiments were conducted by me in the physiological laboratory of the College of Physicians and Surgeons (Columbia University) in the spring and fall of 1897.

As it was desirable to employ animals of some size, dogs were chosen for the experiments.

The irrigating fluid consisted of normal salt solution (one drachm of salt to a pint of water).

I employed one of my double-current rectal irrigators of hard rubber. The fountain syringe was attached to the central tube, and a piece of soft-rubber tubing to the curved carry-off tube. The rectal tube was of infant size. The outflow was so regulated that high irrigation was given. The method has already been described. The first series of experiments was "on the effect on pulse tension," by irrigating at different degrees of temperature. A number of experiments were performed, in order to exclude errors from an idiosyncrasy in any special animal. The average quantity of morphine injected in each dog was about a grain and a half. Ether was employed in addition, when necessary, but in as small an amount as possible. A manometer was connected with one of the femoral arteries, generally the left, and a kymograph attached. The normal blood pressure was noted in each case. This differed somewhat in the animals. Intestinal irrigation was then begun with normal saline solution, and carried on at varying temperatures. Each irrigation averaged ten to fifteen minutes. The following paragraphs give the average result of all the experiments:

Effect on Pulse Tension.—Temperature, 100° F. Slight pressure increases; in a few animals so slight that it *could hardly be detected.*

Temperature, 101°–102° F. Slight pressure increase; a trifle more than above.

Temperature, 102°–104° F. Pressure increasing slightly over above.

Temperature, 105° F. Pressure increases more markedly.

Temperature, 105°–110° F. Pressure increasing progressively with the temperature.

Temperature, 110° F. A *sudden marked* pressure increase; respiratory curve changes; respiration rapid.

Temperature, 110°–120° F. Very *marked* rise of pressure, progressively increasing; pulse very full; heart action strong. This degree of heat most markedly increases tension and stimulates the heart.

Temperature, 90°–60° F. Increase of pressure.

Temperature, 60°. Iced water (this average 36°–37° F.). Marked increase of pressure, this becoming greater as the cold increases.

Note.—After twenty to twenty-five minutes' irrigation with the lower temperatures, the *heart action becomes weaker* and the *pressure* falls.

Deductions.—I. Irrigate at 100°, 101°, 102° F.; or even to 103°–104° F., if increase of pulse *tension* is to *be avoided.*

Though *physiologically* a slight pressure increase is noted at 100°–101° F., and slightly greater at 102°–104°; clinically, in practical use, no increase in pulse tension can be detected after the employment of the above temperatures.

II. If moderate increase in pulse tension is not objectionable, a temperature of 105°–108° F. can be employed.

III. If it is desired to rapidly increase pulse tension and to stimulate the heart, irrigate with a temperature of 110° F., and increase it steadily to 120°. This is excellent in shock and allied conditions; before or during severe operation, to prevent shock, and from the commencement of chloroform anæsthesia, to prevent the sudden dilatation of the vessels.

IV. Cold is a temporary stimulant, and cold irrigation will for a time markedly increase the pulse tension; later it is a depressant, and the pressure falls. Cold should therefore be employed with caution. Clinically, it has been noted that more patients have an idiosyncrasy to cold than to heat.

The high temperatures, 110°–120° F., having thus evidently a powerful effect in increasing the pulse tension and the action of the heart, I next proceeded to make a series of experiments as regards the value of such irrigation in cases of severe hæmorrhage from accident or operation.

This second series may therefore be entitled The Effect of Irrigation on Shock from Hæmorrhage.

The animals were anæsthetized with morphine and a small amount of ether, and manometer and kymograph attached to one femoral artery. I noted the respective pulse tension in each animal, and then withdrew blood from the opposite femoral, watching the effect on the pulse tension and heart. The blood in each experiment was received in a vesel and afterward measured. My object was not to secure a definite relation between the blood withdrawn and the weight of the animal, but to create a severe condition of shock from hæmorrhage by this means, and to demonstrate clearly the great value of irrigation with hot saline of high temperature in this condition. In my endeavor to produce a nearly moribund condition I promptly killed several animals from excessive hæmorrhage. I secured, however, a very hardy Newfoundland, weighing about twenty pounds.

In this animal the normal blood pressure was 155 mm. I then bled him from the right femoral, removing about fifty cubic centimetres at a time, until five

hundred and nine cubic centimetres in all had been removed; the pressure fell rapidly to 112 mm., the animal appearing moribund and nearly exsanguinated. I had already prepared a normal salt solution at 110° F., and rapidly inserted the irrigator and started the flow. The temperature of the fluid was increased to 120° as rapidly as possible. In ten minutes the pulse tension had risen to 140 mm. and was steady at that point, and the heart was acting with fair force. I found it an easy matter to demonstrate the good effects of such irrigation in severe hæmorrhage, but desired to secure an extreme case for the purpose of securing the most marked results possible.

To tabulate: Normal blood pressure, 155 mm.; blood pressure after hæmorrhage, 112 mm.; blood pressure after saline irrigation rises to 140 mm. in ten minutes.

Deduction.—Irrigate with normal saline solution, 110°–120° F., in shock from hæmorrhage.

Note.—The value of the double-current method is self-evident. The patient receives a continuous enema at the desired temperature, and the quantity of the fluid can be absolutely regulated by the operator. The advantages of continuous heat in shock or hæmorrhage are too well known to be discussed.

The effect produced on the temperature of the body and blood by continuous irrigation at various temperatures of heat or cold is of importance. My third series of experiments were in this direction, and may be entitled The Effect of Irrigation on Temperature.

A number of experiments were conducted.

The dogs, as usual, were placed under the influence of morphine and a slight amount of ether.

In some animals a clinical thermometer was inserted

in the left common iliac artery—the tip of the thermometer lying flush with the wall of the abdominal aorta, but not projecting into it. The thermometer was tied firmly in this position. In these animals laparotomy, of course, was performed. In others, clinical thermometers were inserted in the left common carotid, the tip lying flush with the wall of the main vessel at the commencement of the carotid, and firmly tied in this position. All the animals were dissected later to demonstrate that no clotting occurred which could interfere with the experiments. In addition, in some animals the manometer with kymograph was attached to the femoral artery on the opposite side of the body to the iliac artery, in which the thermometer was inserted.

Incisions were made in the axillæ, and clinical thermometers inserted here to secure the average temperature of the body before irrigation, and the changes of temperature as a result of the experiments. All the animals were uncovered, and in a room of about 72° F.

Before irrigation: Axillary temperature averages 99°–99.5° F.

Temperature of the aortic blood averages 102.5°–103.5° F.

Normal pressure noted in each animal. This *varied* 125 mm. to 150 mm.

A period of about fifteen minutes was allowed to elapse before irrigation, to be certain that the anæsthetic had no influence on the temperature.

Irrigation for twenty minutes with normal saline solution at 110° F., increasing to 120°.

There was a gradual rise of temperature; axillary temperature increased 1° F.; temperature of aortic

blood increased 0.5° to 0.8°. Pulse tension markedly increased.

Irrigation was then suddenly changed to cold saline solution—iced water (averaging 36°–37° F.)—and this was continued for twenty minutes, with the following result: Axillary temperature fell 2° F.; blood temperature fell 1° F. Pulse tension at first continued high, later fell, and heart became rapid and feeble.

The experiments with these two extremes of heat and cold were performed on the same animal to make the contrast more marked.

The cold irrigation overcame the increase of temperature caused by the hot irrigation and reduced both axillary and blood temperatures to subnormal.

Temperatures of the irrigating fluid at 100°–105° F. had *no influence* on the temperature in twenty minutes, or at least none that I could discover after careful investigation.

Temperatures of 105°–110° F. caused slight increase of temperature in twenty minutes.

Temperatures of 90°–60° F. in twenty minutes caused no appreciable change in the animal's temperatures.

Below 60° F. there was some loss of temperature in twenty minutes, but not marked until the extreme degrees of cold were reached. There were idiosyncrasies in the animals. One hardy dog in particular seemed hardly at all affected by extremes of heat or cold, and another was especially susceptible. The above results are an average of about eighty per cent. of the experiments.

N. B.—It has been noted that dogs when covered and anæsthetized with ether have an increase of tem-

perature from the anæsthetic when in a room of about a temperature of 72° F.

Now, dogs have no sweat glands except rudimentary ones in the paws, and this fact readily accounts for the phenomena exhibited by these animals during the heat of summer. When the animal is covered, no heat dissipation from the surface of the body is possible; ether is primarily a stimulant, and the increase of body temperature is thus readily understood. In my experiments the animals were thus purposely left uncovered, and the axillary and blood temperature carefully noted within three minutes after the thermometers were tied in the vessels. A period of ten to fifteen minutes was allowed to elapse before irrigation was begun. There was no change in temperature during this period. This corresponds to the result found by other experimenters, who have found that the temperature of the *uncovered* animal in a room at 72° F. is not increased by the ether.

Irrigation was then begun at 110° and increased to 120° F., and in ten minutes a gradual rise was noted, which had further increased at the end of twenty minutes, as stated. The effect on the temperature was thus unquestionably due to the hot saline.

The extreme cold, when prolonged, always reduced the temperature. It was at first stimulating, but later depressing.

Deductions.—I. Hot irrigation, 110°–120° F., when prolonged, increases the temperature of the body and blood. The increase of blood temperature is possibly due in part to the contiguity of the solution to the great vessels, as there does not seem to be a proportionate ratio of increase of the temperature of the body to that of the blood if due merely to effect on heat centres. In

other words, the influence on the blood temperature seems to be greater in proportion than it does on that of the body. The heated blood would undoubtedly be of value in stimulating the heart, and this shows the further advantage of irrigation at a high temperature in shock and allied conditions.

If the patient's temperature is already high, it might be dangerous to irrigate with fluid at a high temperature for fear of increasing the temperature of the patient.

III. Cold irrigation reduces temperature, but is depressing after twenty to twenty-five minutes. At first, cold acts as a stimulant.

IV. Clinically, irrigation at a high temperature has proved to be excellent in shock and allied conditions, as stated above. Chapin, of this city, has employed cold enemata in the diarrhœas of children to aid in the reduction of temperature, and with success. Cold irrigation has also been employed in dysentery for this purpose with good results. Cold irrigation might be employed in sthenic cases to reduce temperature, if used with caution, for five to ten minutes. Friction of the limbs during its application would be advisable, as during the Brand bath. I should not myself care to employ at the start a temperature below 60°–70° F. I refer here to high intestinal irrigation. It would probably be safer also to use it at first only two to three minutes.

On the other hand, I have seen benefit in jaundice (duodenal) from the cold irrigation briefly employed (two quarts), or from the alternate hot and cold douche (two quarts each) for chronic constipation.

A glass Y-attachment, as suggested by Dr. John Minor, of this city, is suggested for this purpose.

Cold rectal irrigations are much safer, and I have seen iced water so applied for thirty minutes in a congestive condition of the rectum, and with great benefit. Some, however, have a marked idiosyncrasy to cold of any degree, and it should therefore be employed with caution.

Hare reports a rise of 4°–5° F. in dogs after twenty minutes' irrigation, with a temperature 115° F.; also a marked fall of temperature, practically shock, after the use of cold for twenty to thirty minutes. He does not state whether or not the animal was covered, or the temperature of the room; which facts make a considerable difference, as previously explained. My own experiments agree with his, as regards the cold, but differ in *degree,* as regards the effect of the heat on the temperature—quantitatively, not qualitatively, in the result. I believe that without doubt the prolonged irrigation has, at the high temperatures, an influence on the body temperature, even though I may be in error as regards the amount of such increase. The cold irrigation, when prolonged, is undoubtedly depressing.

My fourth series of experiments were on the effect of irrigation at different temperatures on the secretion of the kidneys, and the length of time it requires for intestinal absorption to occur. *Other conditions remaining the same,* the secretion of the kidney varies with the quantity of blood flowing through it—the greater the quantity of blood, the greater the secretion.

The blood flow through the kidneys, and therefore their secretory activity, may be affected by conditions influencing general arterial pressure. The condition of the renal circulation itself, and also its relative condi-

tion as regards the general circulation, have an important bearing on the subject. Reference is here made to *An American Text-book of Physiology,* edited by William H. Howell, in the chapter on Secretion. The internal administration of water, in addition to external application, is of great importance in many cases of renal disease, and the employment of enemata or intestinal irrigation for their influence on renal secretion in some conditions has proved of undoubted value.

A number of experiments were performed on dogs. Morphine was injected, and a small amount of ether employed. Laparotomy was performed and the ureters were catheterized. One ureter was so attached that the drops impinged on a lever, which regulated a pen so that each drop was marked on the revolving drum of a kymograph.

The drops from the other ureter were caught in a vessel. In some of the animals a manometer and kymograph were attached to one of the femoral arteries, so at the same time to secure the blood pressure.

Irrigation with normal saline solution at 100°–120° F.

Temperature, 110°–120° F. Increase of renal secretion in *ten minutes,* very *marked in twenty minutes.* Very marked increase of pulse tension. Tension rose at once.

Temperature, 100°–102° F. No increase in renal secretion noted until *twenty minutes*—then is considerable. Slight increase in tension—in some hardly noticeable.

Temperature, 102°–105° F. No increase in renal secretion until *twenty minutes.* Pulse tension slightly greater than above.

Temperature, 105°–110° F. At the higher temperatures slight increase in *ten minutes;* at the lower temperatures *no increase* until *twenty minutes.* At all the temperatures, 105°–110°, considerable increase in *twenty minutes.*

Five cubic centimetres of a five-per-cent. solution of ferrocyanide of potassium were added to about a quart of the irrigating fluid, and the return fluid was caught and employed over again several times. In other animals, repeated irrigations in each animal with a five-per-cent. solution of potassium ferrocyanide, five cubic centimetres in each quart of the saline, were employed. In these experiments the urine as it came from the ureter was tested every minute with chloride of iron. In *twenty minutes* the urine gave the Prussian-blue reaction. This was the average length of time, whether the temperature of the irrigating fluid was 100° or 120° F., or the intermediate temperatures.

Deductions.—I. In *ten minutes* irrigation at the higher temperatures, especially 110°–120° F., stimulates the kidneys to secretion by the heat and by the stimulating effect on the circulation also by the heat, blood flow through the organs.

II. In *twenty minutes,* irrigation at 100°–120° F. causes excretion from the kidneys actually through absorption from the intestines, as is shown by the potassium-ferrocyanide experiments.

III. If possible, if the temperature or pulse tension is not too high, irrigate at the higher temperatures, 110°–120° F. This seems to act in a double way: by the stimulating effect on the circulation also by the heat, and by absorption of fluid from the intestine.

The lower temperatures, 100°, 102°, 104° F., seem

less powerful, and to act more through absorption. There is some increase in tension, as noted in the experiments; but in some very slight. *No increase* in secretion of urine could be discovered until *twenty minutes* had elapsed, and this was shown by the potassium ferrocyanide experiments, which gave the reaction at that time. The slight increase in tension would not seem to account for the renal secretion in this case.

For the most part, it could justly be imputed to absorption from the intestine. Clinically, irrigation at 100°, 102°, 104° F. has increased renal secretion, without any discoverable increase in pulse tension. Repeated small saline enemata have produced increased renal secretion without perceptible change in tension. I mean enemata of two to three ounces at 101° F.

IV. If it is desired to increase renal secretion without increasing pulse tension or temperature, irrigate at 100°–104° F., and at 105°–108°, if moderate increase is not objectionable.

V. Intestinal absorption from the large intestine occurs in *twenty minutes.* This has an important bearing on self-infection. Hence the value of irrigation in diarrhœas.

Note.—Dr. L. Bolton Bangs has administered enemata of iodide of potassium and secured reaction in the urine in *twenty minutes.*

VI. *Clinically.*—Hot saline irrigation is an excellent remedy in acute uræmic suppression, or in cases of renal insufficiency.

Dr. Egbert Grandin, of this city, has had excellent results from this procedure, and has been advocating it for some time past. Dr. William H. Thomson has em-

ployed it with success when other means have failed. They both report excellent results, profuse sweating and bowel action accompanying the renal secretion. Dr. Thomson has employed saline irrigation at 101°–104° F. with gratifying results recently in an obstinate case of renal insufficiency where other remedies were a failure.

Renal disease with polyuria as a symptom would seem to contraindicate this method, or that it should be cautiously used and for short periods. This statement has special reference to a case of enlarged prostate, in which prolonged irrigation was employed. It aggravated the polyuria and had to be stopped.

Note.—It will be specially noted that no reference has been made to the effect of cold irrigation on renal secretion or intestinal absorption. Some have advocated cold enemata in renal suppression; but I consider it a dangerous procedure. Experiments were made in this regard, but I purposely place them apart. Enemata of cold water at different temperatures will be absorbed from the intestines and, as in experiments with hot saline with potassium ferrocyanide, urinary reaction will occur in about twenty minutes, giving the blue with chloride of iron. On the other hand, *cold irrigation* will for a short time stimulate the circulation and increase secretion, but in about *twenty minutes* pulse tension will fall, the animal will go practically into shock, and renal secretion *cease*. We will thus have renal suppression plus shock, or be worse off than before, and the cold will aggravate the suppression.

A small quantity of cold water was employed in the enema, and the absorption easily demonstrated. Notice one experiment by enema, the other by irrigation.

Cold irrigation I would believe to be absolutely contraindicated in *renal disease*—also cold enemata.

The *cold* irrigation would practically inhibit intestinal absorption on account of the effect on the circulation at the end of twenty to twenty-five minutes. This explains the apparent contraindication.

Now physiological experiments and the clinical application of them do not always agree. In the deductions as to temperature it will be noted that irrigation at 110°–120° F. was recommended when the *pulse tension* or *temperature* was *not high*. The nature of the case, the age of the patient, and many other conditions are to be considered. I have seen excellent results in acute uræmic suppression, with considerable pulse tension and a temperature of 102° F., from a twenty-minute irrigation at 110°–115° F., with profuse diuresis, sweating, and bowel action as a result, and a fall of pulse tension and temperature.

Every case should be taken on its merits. The above-mentioned case was in a young person. If the vessels are atheromatous, a great degree of heat would be unsafe.

Being desirous of comparing the time required for renal excretion after intestinal irrigation with that after hypodermoclysis and infusion, I conducted two more series of experiments.

My fifth series was on hypodermoclysis. A dog was placed under the influence of morphine and a small amount of ether. Laparotomy was performed and the left ureter catheterized. The urine was conducted from this into a small glass vessel.

Five cubic centimetres of a five-per-cent. ferrocyanide-of-potassium solution were added to about three

ounces of a normal salt solution at 104° F. This was injected with a large syringe into the tissue of the right groin. The urine was tested every fifteen seconds with chloride of iron. In three minutes and a half the Prussian-blue reaction was noted, which became marked in four minutes. *Renal secretion* slightly increased.

Deductions.—This method would thus be of value: 1. In shock. 2. In shock from hæmorrhage. 3. In cholera, to replace loss of fluid and dilute poison. 4. In acute uræmic suppression, to start up secretion and dilute poison, etc. It has so been recommended, but I believe that it should be more frequently employed, as it is a valuable adjunct.

My sixth series of experiments was on infusion. A dog was placed under the influence of morphine and a small amount of ether. Laparotomy was performed, the left ureter catheterized, and urine received in a small glass vessel. One cubic centimetre of a five-per-cent. potassium-ferrocyanide solution in three drachms of normal saline solution at 110° F. was infused slowly into the right femoral vein. The urine was tested every fifteen seconds. In a minute and a half to two minutes Prussian-blue reaction in urine with chloride of iron. *Renal* secretion slightly *increased.*

Note.—In 1891 Dr. Robert Dawbarn, of this city, conducted a series of experiments on dogs at the College of Physicians and Surgeons as regards the proper temperature of infusion. He found that saline solution at 115°–120° F. best stimulates the heart. He employs infusion of saline solution for cases of shock at this temperature and was the first to suggest and likewise employ such infusion *before severe operation* to *prevent shock.* In the course of his experiments he

found infusion of sterile water (plain) killed the animals by destroying the red cells.

These experiments are here noted as of great importance in connection with infusion.

My own experiments on infusion were in regard to the length of time it takes for renal secretion to occur. Some claim it occurs as soon as a minute *after infusion.* My experiments with *irrigation* also show that 110°–120° F. temperature best stimulates the heart.

Comparison.—Infusion: Renal secretion occurs in a minute and a half to two minutes.

Hypodermoclysis: Renal secretion occurs in three minutes and a half to four minutes.

Enteroclysis: Renal secretion occurs in twenty minutes.

On Infusion: Deductions from Dawbarn's Experiments.—I. High temperature of saline solution, 115°–120° F., is the best stimulant—(*a*) in shock; (*b*) in shock from hæmorrhage; (*c*) before severe operation, to prevent shock, or to prevent dilatation of vessels in chloroform anæsthesia.

On Infusion: Deductions from Kemp's Experiments.—I. Useful in some cases of acute uræmia to dilute the poison and cause renal secretion.

Note.—This method has been reported as successful in some cases; especially, a definite amount of blood being first withdrawn by venesection and replaced by saline solution. It was first performed abroad.

The technique of infusion is more difficult than that of the other methods, and the instruments must be perfectly sterile.

For hypodermoclysis a proper needle can not always be secured.

Irrigation with two catheters or a double-current tube is extremely simple. It acts rapidly in shock and other conditions of a like character. It is well to start the irrigation while preparing for the other methods.

Some Further Observations on Irrigation.—On account of the length of my article I shall reduce my remarks to rather an epigrammatic style. I have found the following four tubes to practically fulfill all the clinical indications.

No. ½. Hard-rubber double-current rectal irrigator (adult size).

No. ½. Metal double-current rectal irrigator (adult size). This is described in the *Medical Record,* July 24, 1897. A rubber collar will protect the sphincter if heat is complained of. The tube is durable and can be boiled.

Soft-rubber double-current rectal irrigator, with a metal centre, also adult size. This can be bent to suit, and is excellent in cases of enlarged prostate or uterine tumor partially obstructing the rectum.

Note.—If the tube does not slip readily into the rectum, always examine to see if there is an obstruction.

Soft-rubber double-current rectal irrigator (flexible), also of adult size. This is excellent in sensitive cases, or in *infants* and *children.* For infants it can be thoroughly softened in hot water and inserted only part way. It gives a better current than the small infant tubes. At times I employ the flexible rectal tube for infants.

The flexible tubes are readily injured, especially if left in solution The central tube is generally made of a linen catheter. I have found the flexible English

catheter (such as has the stylet) much more durable. The ends do not fray as readily, nor does it crack as easily. No. 7 is a good size. It can be cut in lengths to suit, and the hard-rubber fittings will cut their own thread on it.

The flexible short tubes or colon tubes should be cleaned as follows: Unscrew the accessory cap and loosen the main cap, pushing them along the central tube to nearly its end; then withdraw the hard-rubber tip from the main outer tube, and with it about half an inch of the central linen tube; then unscrew the tip and withdraw the central tube, as in the other instruments. If the attempt were made to unscrew the flexible tube as in the other instruments, it might be easily torn through.

The flexible tubes should not be allowed to remain in any solution, except for a moment, as the centre tube readily softens and collapses. Should this occur, a wire passed through the central tube will generally remedy the difficulty.

I have found the following the best method, as the curved (lateral) tube is the larger in the calibre, and gives a better outflow:

Method of Attachment.—If the fountain syringe is attached to the central tube and the carry-off tube to the lateral tube, the current seems more forcible. A short soft-rubber tube is attached to the curved tube. By alternately pinching this and the tube of the fountain syringe the quantity of fluid entering and escaping can be regulated. Avoid pressing the tip of the instrument against the wall of the bowel, or directing the current against it, as either is irritating.

Normal saline solution is preferable to plain water,

as it does not dry the mucous membrane or injure the epithelium.

Insertion of the Instrument.—1. The tube should be well lubricated and inserted with a gentle rotary movement, not forced in; this is especially the case with the hard tubes.

2. If the flow ceases, rotate the tube slightly, or withdraw it slightly and push it back. If the return tube seems plugged, attach the fountain syringe to it for an instant, and force the current in the opposite direction.

A small, hard-rubber rectal syringe (enema), which contains from half an ounce to an ounce, is excellent to clean the outflowing tube. Shut off the entering current, and then force water back into the bowel through the outflow tube. This will clean it.

3. Insert the rectal tube about a third to half its length in prostatic cases, etc., and full length for high irrigation.

N. B.—Clinically, the rectal tube, inserted full length, and the patient with hips elevated, seems to be satisfactory, even in high irrigation, as in colitis, etc., though some prefer the colon tube.

The mehod by rotation, described March 13, 1897, by percussion, and succussion, proves that the caput coli can be irrigated with the short tube if proper advantage is taken of the patient's position.

Dr. Egbert Grandin states that he has seen the fluid pass through the large intestine to the caput coli and back through the bowel (large), in other words, a continuous irrigation of the entire large intestine. This was performed with saline for shock during laparotomy; the hips were elevated, and hot saline employed. The

patient was emaciated and the intestinal wall extremely thin. The five-inch tube was used in this case. This is certainly an absolute ocular demonstration.

In self-irrigation of the prostate I have found the following method convenient: Hang the fountain syringe about a foot above the level of the patient's head and on the left side; attach the tube of the fountain syringe to the central tube and an inch of soft tubing to the curved tube of the irrigator. Insert the irrigator about half its length, the curve tube looking toward the perinæum. The central tube of the irrigator passes between the middle and ring fingers of the left hand; the index and middle fingers support the curved tube of the irrigator. The patient leans somewhat forward, as if to have a movement. The wrist is supported by the left buttock. The index or middle fingers respectively regulate the inflow and outflow by bending a kink in the soft tubes. The clip is thus unnecessary.

The accompanying cut shows the rectal metal irrigator ready for cleansing. The other instruments can be taken apart equally well.

I have found the Sims posture, with the *shoulders elevated,* to be excellent in prostatic cases when an attendant performs the irrigation. Prolonged irrigation is necessary in these cases.

Dr. Robert W. Taylor, in his recent work on *Sexual Disorders of the Male and Female,* advises it in a certain class of cases in combination with massage of the prostate.

I should state that Dr. Poncet, of Vichy, France, is at present experimenting with the methods described in the *New York Medical Journal* of March 13, 1897, and I believe is the first to employ the double-current method in France.

In closing, I wish to express my thanks to Professor Curtis and Professor Lee for the facilities afforded me at the physiological laboratory, and for the uniformly courteous treatment received at their hands. I have also to thank Dr. William H. Thomson, of this city, for some valuable suggestions made in regard to the experiments. I am perfectly aware that enemata of water have been used for some years to promote renal secretion and dilute the poison of disease, to alleviate shock, and reduce temperature. An obturator invented by Dr. David Prince, and reported in 1883, is shown in Tiemann's *Catalogue.* This is to retain enemata for the purposes mentioned. Intestinal irrigations have also similarly been used, and the double-current principle was employed before I was born. I know that experiments have been made in regard to intestinal absorption and the effect of irrigation on body temperature (eee Hare). However, as regards the method of the insertion of thermometers in the large vessels, the experiment on hæmorrhage with continued irrigation, and the results on renal secretion produced in varying degrees by the different temperatures, so far I have not been able to find similar experiments. If they have been previously performed I offer my apologies at once. The

longer I live the more ready I am to believe that "there is nothing new under the sun." I trust, however, that my efforts here published will induce others to investigate these most interesting questions and to correct the errors I may have made. Progress is the result of investigation, and necessarily of controversy.

444 Park Avenue.

Studies from the Department of Physiology of Columbia University, at the College of Physicians and Surgeons, New York.

Reprinted from the American Journal of Physiology, Vol. I, 1898.

THE FUNCTIONS OF THE EAR AND THE LATERAL LINE IN FISHES.[1]

By FREDERIC S. LEE.

[*From the Physiological Laboratory of Columbia University, at the College of Physicians and Surgeons, New York.*]

ALL vertebrate morphologists are well aware that two of the prominent vexed problems of their science are the history, ontogenetic and phylogenetic, of the ear and that of the system of sense-organs usually called the sense-organs of the lateral line, a structure found in Fishes and aquatic Amphibia, larval or adult. Into the differences of opinion and confusion in this field of research Beard,[2] in 1884, introduced a semblance of order, and at the same time gave cause for much further contention, by bringing the two organs, or systems of organs, together phylogenetically, and claiming the ear to be nothing more nor less than a modified portion of the system of the lateral line. Since then much has been written upon this phase of the subject, the chief single contribution, perhaps, being that of Professor Ayers,[3] who adopted and developed very fully the general idea suggested by Beard.

The chief morphological facts upon which this view is based, are, in brief, the following: —

1. *Similarity in ontogeny.* — The ear and the lateral line seem to develop from a common ectodermal thickening, which extends forward and backward from the place of origin.

2. *Similarity in structure of adult organs.* — It is now generally acknowledged by morphologists that the internal ear is not one organ, but a group or system of organs, comprising in the fully developed ear of the fish seven recognizable patches of sensory epithe-

[1] The substance of this article was presented before the Section in Physiology of the British Association for the Advancement of Science at its meeting in Toronto, August 19, 1897.

[2] Beard, J.: On the segmental sense-organs of the lateral line, and on the morphology of the vertebrate auditory organ. Zool. Anzeiger, 1884, vii, p. 140.

[3] Ayers, H.: Vertebrate cephalogenesis. II. A contribution to the morphology of the vertebrate ear, with a reconsideration of its functions. Journal of morphology, 1892, vi, p. 1.

lium: the three cristæ acusticæ, contained in the walls of the ampullæ of the semicircular canals; the three maculæ acusticæ, contained in the recessus utriculi, sacculus, and lagena; and the rudimentary macula neglecta, contained usually in the utriculus. The structure of these is well known; in each there is a localized area of sensory epithelium, supplied by special nerve-fibres and consisting of hair- and supporting-cells. The processes of the hair-cells project into a liquid, the endolymph. In addition to these parts, common to both cristæ and maculæ, each macula bears a mass of otoliths, resting upon the sensory hairs. The labyrinthine cavity of the internal ear in the Selachians is more or less freely open to the outside medium through the ductus endolymphaticus.

The sense-organs of the lateral line are numerous, and are either free or contained in canals lying in the skin of the head and the sides of the body. These canals are open at intervals directly to the water of the medium, as are the semicircular canals through the endolymphatic duct. From their position, different portions of the lateral system have received the names supraorbital, infraorbital, mandibular, occipital, and lateral. The structure of the sense-organs closely resembles that of the cristæ acusticæ: in each there is a localized area of sensory epithelium, supplied by special nerve-fibres and consisting of hair- and supporting-cells; the processes of the hair-cells project into a liquid which, when canals are absent, is the water of the medium, and, when canals are present, is this water plus more or less mucus excreted by the cells lining the walls of the canals.

3. *Similarity in innervation.* — The sense-organs of the lateral line are innervated by nerve-fibres forming well-marked bundles, which run to the periphery usually in company with branches of the fifth, seventh, ninth, and tenth cranial nerves. To speak of them as being innervated by these cranial nerves is misleading; the connection of their nerves with the cranial nerves is secondary. In reality, the nerves of the lateral line form a definite system of their own with a common central origin, which central origin is, likewise, the central origin of the eighth or acoustic nerve.

It must be acknowledged that these facts are of great importance, and seem to warrant the interpretation given to them.

Can physiology throw any light upon this question? A study of function is not usually believed to be capable of elucidating the genetic relationship of organs, and hence most writers have wholly neglected the physiological side. It might have been advantageous if

more had done this, for the physiology that has thus far been introduced is largely speculative, usually lacks an experimental basis, and is at times grotesque. What is needed here, as in all similar cases, is not speculation from morphological facts as to function and the origin of function, but reasoning from physiological facts that are first acquired by rigid and critical experiment. We have here an admirable opportunity to demonstrate not only that the phylogeny of function is worthy of study for its own sake, but that physiology is at times able to present, if not direct, at least valuable circumstantial evidence of the truth of morphological deductions. The evidence that I wish to bring forward has been obtained, unless otherwise stated, by myself from experiments upon fishes at the Marine Biological Laboratory, Woods Holl, Mass., during recent summers. The form chiefly used was the common smooth dog-fish (Galeus canis, Mitchill) of our Atlantic coast.

Some of the results have already been published, but must be mentioned briefly in this connection for the sake of rendering the subsequent work more easily understood. No attempt will be made to discuss the experiments of others upon higher animals, as this for my present purposes would be quite superfluous. The work is not yet completed.

We will consider the functions of the various sense-organs in order.

I. The Ear.

A. **The cristæ acusticæ.** — The experiments here have been clear-cut, and the results have appeared with a mathematical exactness rarely realized in physiological investigation.

One general function is here present, namely, the appreciation of rotary movements of the body, *i. e.*, movements in curved lines. Hence, the semicircular canals with their sense-organs are organs of equilibration.

The methods of arriving at this conclusion were three: turning the normal fish in the planes of the canals and other planes; stimulating separately and in combination the various ampullar branches of the acoustic nerve, which in the fish are separate and very easily reached; and cutting these ampullar branches. The index to the state of the animal's sense of equilibrium was found in the compensating movements of the eyes and the fins. The results obtained by these three methods are entirely harmonious. Thus, turning the normal

animal in a definite plane, either the plane of a canal or a plane between two canals, causes the eyes and fins to make certain definite and constant movements, which indicate a recognition of the body-movement and an attempt to resist or overcome it. If, now, the canals of the corresponding planes be exposed in another animal, and their cristæ stimulated artificially, exactly the same compensating movements of eyes and fins are made. The inferences are: first, that the operated fish has the sensation of being turned out of his normal position; and second, that when a normal fish turns in the planes specified, he stimulates the corresponding cristæ. This latter inference is corroborated by cutting the nerves supplying the cristæ in question, and then turning the animal in the same planes as before. This has not been done for single cristæ, and it is quite possible that in such case the others would maintain the compensation; but it has been performed for a functional pair of cristæ, and the result is absence of the normal compensating movements pertaining to the canals in question. The harmony of the results of these three methods is striking.

Each canal with its sense-organ has a principal and a subordinate function: the former is the appreciation of rotary body-movements in the plane of the canal and toward its side of the body; the latter is the appreciation of similar movements in the same plane but in the opposite direction. Each canal has a functional opposite, the two lying approximately in the same plane, and the principal function of one being the subordinate function of the other. Such functional opposites are the right anterior and the left posterior, the left anterior and the right posterior, and the right and left horizontal canals. A simple movement of the body in the plane of a canal puts the canal into most complete action; a movement in any other plane may be regarded (from the standpoint of the canals) as a compound movement, and may be resolved into simple movements in the planes of two or more canals. Such compound movements are appreciated by the two or more canals acting as a double organ (functional pair), or triple organ, which likewise possesses its principal and subordinate functions. The action of a functional pair, or double organ, is exemplified in the appreciation of diving movements by the two anterior canals, and in the appreciation of the movement of shooting upward in the water by the two posterior canals.[1]

[1] For a fuller discussion of the functions of the canals the reader is referred to my articles already published. Ueber den Gleichgewichtssinn. Centralbl. f.

B. **The maculæ acusticæ.** — Here not so much work has been done, and the results are not as sharp-cut as in the case of the cristæ. Artificial stimulation of the maculæ has been tried in a large number of cases, but does not appear to give consistent results. Cutting the macular nerves or, perhaps better, removing the otoliths that always cover the maculæ, makes a decided general change in the conduct of the animal, which to one familiar with the movements of fishes seems to indicate unmistakably the lack of certain sensory functions. It should be premised that, in the form studied chiefly, the utricular and saccular maculæ are very closely contiguous, and the macula of the lagena is simply a small continuation of that of the saccule; hence, so far, it has been impossible to separate the three functionally, and it is very questionable whether the division of labor here is as sharp-cut as with the cristæ.

Two functions seem to be present, both of which are equilibrating: the appreciation of translatory or progressive movements, or movements in straight lines, and the appreciation of the position of the body in space.

1. *Appreciation of progressive movements.*[1] — A normal fish has a delicate sense of the distance involved in swimming in a straight line. This is shown by the remarkable skill with which he avoids obstacles; in swimming around his aquarium constantly, he strikes his nose directly against the side of the tank comparatively rarely. This is not so with a fish deprived of all his otoliths or with all his macular nerves severed. Such a fish seems to have little idea of the extent of a forward swim. He is often restless and frequently alters the direction of his progression. In moving along close to the side of a large oblong tank he often swims at his usual rate and with his usual freedom, and appears fairly normal; but, upon reaching the end, it frequently happens that he does not turn, like the normal fish, gracefully to one side and thus avoid the end-wall. On the contrary, he often bumps directly into it. When excited by a stick, he darts about in different directions, irregularly and with awkward,

Physiol., 1892, vi, p. 508. A study of the sense of equilibrium in fishes. Part I. The Journal of physiology, 1893, xv, p. 311; and Part II, *ibid.*, 1894, xvii, p. 192.

[1] A full account of my observations upon this function and upon the subject of hearing in Fishes has not been published. My observations were communicated to The American Physiological Society, 1894, Dec. 28: a brief abstract of that Paper was printed in "Science," 1895, Feb. 1, N. S. i, p. 118, and a still briefer one in the Centralblatt für Physiologie, 1895, April 6, ix, p. 47.

uncertain, and ill-regulated movements, often shooting far out of the water. Moreover, after swimming into a corner, his movements are awkward and he finds great difficulty in retreating or getting back into open water. If he succeeds in doing this, he may return at once to the same corner and repeat his ungainly attempts at extricating himself. It is easy to draw a hasty inference that the eyesight of such a fish must in some mysterious way be at fault. As a matter of fact, however, a fish deprived of his eyesight, but in other respects normal, does not conduct himself in that way. When left to himself, the blinded fish[1] swims normally in all respects, moving gracefully, easily, and without timidity, and shooting and diving like an uninjured fish. When disturbed by being poked he darts about with great rapidity, but is master of his movements. In the first few hours of his blindness he bumps the end of the tank in progressive swimming, but soon he largely overcomes this, and, probably by his sense of touch, learns to avoid gross contact with such obstacles. He then touches the walls lightly, glides away from them easily, and only when disturbed bumps as at first. When by chance he swims into a corner, he extricates himself easily, gracefully, and with certainty. The compensating movements of his eyes and fins are entirely normal.

It is thus seen that the fish deprived of retinal sensations and the fish deprived of macular sensations act very differently. The conclusion that in the latter animal the appreciation of progressive movements is dulled or largely eliminated seems quite sufficient to explain the phenomena.

We thus find experimental proof — and the first thus far reported in animals lower than man, if I am not mistaken — of the presence in the otolithic parts of the ear of a power to appreciate progressive movements. That such a function must exist there was ably advocated by Breuer,[2] who gave reasons for the probability "that the perception of rectilinear movements is sharper in Fishes and Birds than we find it in observations on ourselves."

2. *Appreciation of position in space.* — The fact that a normal fish has a delicate sense of his position in space, of upness and downness, is demonstrated by the difficulty experienced in inducing one to rest

[1] In blinding, the contents of the eyeballs, including the retinas, were removed; the sclerotic coats with their muscular attachments were left *in situ*.

[2] Breuer, J.: Ueber die Function der Otolithen-Apparate. Arch. f. d. ges. Physiol., 1890, xlviii, p. 195.

in any other position than that with the back upward and the belly downward. He not only resists with all his powers being turned over (this movement is appreciated by the semicircular canals), but with equal energy he resists being compelled to remain out of his customary position; and, when put out of the latter and then left to himself, he at once assumes his normal attitude.

It is not so with a fish from which the otoliths have been removed, or in which the macular nerves have been cut. If either of these operations be done upon one side only, the eyes and fins are placed in abnormal positions; in reclining, the operated side is usually slightly downward; normal swimming is possible, but here usually the operated side is depressed; when disturbed, the fish usually darts off with that side downward; and in coming to rest he often loses his balance and sinks down flat upon that side, never upon the other. If the operation be performed on both sides, the fish seems to have largely lost his sense of upness and downness. While preferring usually the normal attitude, it is not difficult to make him remain lying on his back or side; and not rarely he is found in such abnormal positions, having assumed them himself. He swims at times upon his side, and occasionally upon his back. He seems not to appreciate at all clearly his position in space.[1]

I have found no reason to disbelieve that the same otolithic parts of the ear appreciate both progressive movements and position in space, which is not in accordance with the doctrine of specific energy in its extreme form. The view of Breuer,[2] however, seems wholly reasonable, namely, that changes in the pressure of the otoliths are appreciated as changes of position in space when they are accompanied by sensations (ampullar) of rotary movements, and as progressive movements when not so accompanied.

It is evident that there is a close functional connection, through the central nervous system, between the sensory organs of the ear, the cristæ and maculæ, and the locomotor organs of the body. A reflex arc with the evident function of equilibration is thus established. The idea that the cristæ and maculæ are sensory organs of this function does not preclude acceptance of the well-established fact that other

[1] For a fuller discussion of this statical function of the maculæ, the reader is referred to the author's articles in the Centralblatt für Physiologie, 1892, vi. p. 508, and the Journal of physiology, 1893, xv, p. 311.

[2] Breuer, *loc. cit.*

sensory organs, such as the eyes, are similarly connected by reflex arcs with the locomotor organs, and similarly functionate as sensory organs of equilibration. In these latter organs equilibration is accessory to other chief functions, as in the eyes to sight; in the cristæ and maculæ it is the chief, and perhaps the only, function.

The functions of the ear of the fish so far considered may be put in convenient tabular form as follows: —

I. Dynamical functions, in recognition of
  1. Rotary movements, mediated by cristæ acusticæ.
  2. Translatory movements, mediated by maculæ acusticæ.

II. Statical functions, in recognition of
  3. Position in space, mediated by maculæ acusticæ.

As to the manner of stimulation, it is evident that both the cristæ and the maculæ belong to the category of pressure-organs. This is most evident in the maculæ, in which the pressure of the otolithic mass upon the delicate sensory hairs affords a constant stimulus which varies in intensity with the position of the animal in space, or with the force of the progressive movement.

In the cristæ, the most reasonable mode of stimulation appears to me to be that due to the inertia of the endolymph as the hair-cells are moved through space along with the body. The result is a greater pressure upon one side of the hairs than upon the other, and hence a stimulation of the sensory cells by pressure.[1]

[1] In a recent article E. v. Cyon (Bogengänge und Raumsinn. Experimentelle und kritische Untersuchung. Archiv für Physiologie, 1897, p. 29) appears in the light of a sceptic regarding the results obtained in my experiments on dog-fishes, apparently because of their exactness and completeness. Among other things he reproaches me with the fact that "Lee hat . . . immer alles bestätigt gefunden, was die Hypothese erheischt." This fact will occasion no surprise, when it is borne in mind that the great majority of my results were obtained long before the "hypothesis" as formulated by myself was made (cf. LEE: Journ. of physiol., 1893, xv, p. 321), and long before I was acquainted with the work of Breuer. The theory as formulated in my chief Paper was a direct induction from the facts obtained by myself; I took pains to keep it within the limits of those facts, and thus it was that I "always found what the hypothesis demanded." In a subsequent Paper (LEE: *ibid.*, 1894, xvii, p. 192) I aimed "to fill in certain gaps that were left in the previous series, to make the proof of certain points more logically complete, and experimentally to verify certain inferences and prophecies resulting from the theory formerly stated." As regards the exactness of my results, I have often felt and expressed surprise similar to that which Cyon apparently feels. Yet I have endeavored accurately to chronicle the phenomena

C. **The question of hearing.** — We thus appear to have found a function for all of the sensory organs of the ear of the fish. But the question naturally arises — does not the fish possess audition? In higher vertebrates, of course, this is present, and we can add to the above scheme:

III. Auditory functions, in recogniton of { 4. Vibratory motions, mediated by papilla acustica basilaris.

This exhausts all possible cases of mechanical (*i. e.* visible) motions in matter. It is interesting that the ear is the sense-organ that appreciates all kinds of visible motion.

Wherever among vertebrates undoubted audition exists, there is present an additional group of sensory end-organs, the papilla acustica basilaris. This does not exist in Fishes, but appears first in the Amphibia as an offshoot from the lagena, and in higher vertebrates constitutes the nervous portion of the organ of Corti of the cochlea.

actually observed under the circumstances of the many and widely varied experiments.

Cyon further seems to regard the integrity of the sense of sight as necessary to the performance of the compensating movements of the eyes, and makes the astonishing statement that "... der Dogfish (Galea canis) tagesblind ist, wie Beer unzweifelhaft bewiesen hat." On the contrary, Beer (Die Accommodation des Fischauges. Arch. f. d. ges. Physiol., 1894, lviii, p. 577) has neither stated nor attempted to prove such a thing. He says: "Wir haben einigen Grund anzunehmen, dass die Pupille der in Freiheit lebenden Fische wegen der relativen Dunkelheit grösserer Tiefen noch etwas weiter sein wird, als bei den Thieren in den gewöhnlichen Versuchsbassins, die in einer für sie vielleicht blendenden Helle leben. Bei vielen Haifischen und Rochen tritt sogar in den dunkleren grossen Aquarien der Station tagsüber eine so starke Miosis ein, dass die Pupille — die Nachts, resp. im Dunkeln sehr weit ist und dann auch hier den Linsenrand sehen lässt — fast gar nicht sichtbar, sondern ... verschlossen wird; die Thiere benehmen sich auch wie blind," etc. As a matter of fact, under the circumstances of my experiments, the pupils of Galeus canis varied greatly in size, from being wide open to being partially closed. But I do not now recall a single instance of their being wholly closed, nor have I ever seen an uninjured individual of this species behaving during the daytime like a blind fish. In an experience of three summers this species has not exhibited himself as "blind in daylight." This question is, however, of minor importance, since, as stated above, the eyeballs from which the contents, including the retinas, are removed, perform the normal compensating movements. Cyon appears not to comprehend the fact accented above, namely, that the movements of the eyes are reflex movements, the afferent stimulus to which comes from the cristæ acusticæ. This does not preclude the further undoubted fact that under normal circumstances the movements are accompanied by sensations of sight.

At first sight the presence of the "ear" in Fishes presupposes a sense of hearing; but the absence of the papilla acustica basilaris argues against it. The fact that fishes, with comparatively few exceptions, are dumb seems to me strong evidence against the possession by them of a sense of audition. It would seem that the primary purpose of the power of emitting sound by an organism is communication with other individuals of its own species. Similarly, the primary purpose of a sense of hearing is apparently the gaining of information regarding the presence of other individuals of one's own species. In each case the employment of the function for other purposes would be secondary. If this be so, we should expect the two powers of emitting sound and of hearing sound to be developed in the same individuals and developed more or less *pari passu*. A survey of the various groups of animals shows this to be the case. Further, it is difficult to conceive upon any grounds the object or usefulness of the possession by Fishes of the power to hear in the sense in which the term is ordinarily used. The depths of the sea are silent, the sounds of the waves probably penetrate only the most superficial layers of the water, and aquatic animals, with comparatively few exceptions, are dumb. Along the shores some outside sounds might penetrate the water superficially, but such would form only a very slight exception to the general law that in nature water, unlike air, is devoid of sound.

But experimentation can best answer the question as to the power of audition in Fishes.

In the summer of 1894 I tested a number of species as to their power of hearing, employing ordinary sounds, such as the human voice, clapping the hands, and striking stones together in the air and under water.[1] I obtained no evidence whatever of the existence of a sense of hearing as the term is customarily employed, although I learned that fishes are exceedingly sensitive to gross shocks, such as the jarring of their tank or concussions upon its walls, *i. e.*, such vibrations as human beings recognize through other sensory mechanisms than the ear as distinct mechanical vibrations. The accompaniment of such apparently gross vibrations was the indispensable condition upon which the fishes in my experiments reacted to sounds. I have learned recently of Bateson's similar experiments[2] which were

[1] See footnote p. 132.

[2] BATESON, W.: The sense-organs and perceptions of fishes. Journal of the marine biological association, 1890, i, p. 225.

interpreted in much the same way. In 1895 Kreidl[1] published the results of a considerable series of experiments carefully conducted upon goldfish. He used as sources of sound in the air various whistles, electric and other bells, clapping of the hands, and the firing of a revolver, and in the water vibrating rods; and he studied their effects upon normal fishes, those whose excitability was greatly increased by strychnine, and those that had been deprived of their ears. Neither normal nor strychnized fishes showed any reaction whatever to musical sounds of any pitch or intensity, produced in the air or water. Concussions, such as striking the walls of the aquarium in the case of normal animals, or clapping the hands or firing a revolver in the case of strychnized animals, produced marked reactions, especially in the latter; but such reactions were equally well-marked after both ears were removed, and still remained after the removal of the whole cerebrum and a portion of the mid-brain. His experiments leave no doubt of the correctness of his conclusions, which were: "(1) That hearing through the 'auditory organ' cannot be demonstrated in the goldfish; (2) nevertheless, they react to sound waves, which they perceive through a specially developed skin-sense."

In a subsequent paper Kreidl[2] explodes the oft-repeated tale of hearing by fishes that come for their food at the sound of a bell, by investigating carefully the actions of trout at the famous old Benedictine monastery in Krems, Austria. He proved that the fishes come because they see the man who brings the food, and appreciate the vibrations of the water caused by his step and communicated through the stone basin; and that, when these are excluded, the sounds of the bell have no effect.

The conclusion seems justified beyond doubt that fishes do not possess the power of hearing, in the sense in which the term is ordinarily used.

We must believe that in vertebrates this sense was evolved along with a change of the mode of life from a water to a land existence, and was contemporaneous with the appearance of a papilla acustica basilaris.

It appears plain that the sole function of the ear in Fishes is equilibration.

[1] Kreidl, A.: Ueber die Schallperception der Fische. Arch. f. d. ges. Physiol., 1895, lxi, p. 450.

[2] Kreidl, A.: Ein weiterer Versuch über das angebliche Hören eines Glockenzeichens durch die Fische. Arch. f. d. ges. Physiol., 1896, lxiii, p. 581.

The mechanism by which Fishes appreciate certain mechanical vibrations and which Kreidl proved not to reside in the ear, is no more understood in them than it is in other animals and in human beings. This power is wide-spread in animals, even in many Invertebrates in which there is an absence of the power of hearing, *e. g.*, in earthworms, and it is astonishingly developed in some human beings. My friend, Professor Hallock, tells me that Helen Keller, who, it is well known, is totally deaf and devoid of other special senses except that of touch, is able, by keeping her fingers in contact with the larynx of a person who is singing, to appreciate accurately the changes in pitch; she can thus accurately reproduce with her own voice the notes sung by her companion. There is no question here of the absence of the sense of hearing, yet the vibrations are appreciated. As regards these two sense-activities, the case of the normal fish is without doubt analogous to the case of such defective human beings.

II. The Lateral Line.

The original view of the function of the lateral line was that its canal produced mucus for moistening the surface of the body of the fish. When in 1850 Leydig[1] discovered the numerous sense-organs in it and later ascribed to them the mediation of a sixth sense, the original view was laid aside for others of a sensory function. Upon little experimental evidence it has been suggested that the organs are true touch-organs, are auditory organs, that they appreciate currents in the surrounding water, the chemical nature of the water, and so on. There has been no consensus of opinion as to their exact function or mode of action.

During the summers of 1892, 1893, and 1894, I carried on at different times experiments of various kinds upon the lateral-line system (not including the ampullæ of Lorenzini or Savi's vesicles). I studied several species of fishes, especially the dog-fish (Galeus canis, Mitchill), the toad-fish (Batrachus tau, L.), and the butter-fish (Stromateus triacanthus, Peck), and obtained certain suggestive results. The main points will be communicated here.

In the dog-fish the lateral-line organs of the head are supplied by the superficial ophthalmic, the buccal, and the hyomandibular branches of the seventh nerve; those of the body by the so-called lateral branch of the vagus. In this species I have cut all of these

[1] Leydig, F.: Ueber die Schleimkanäle der Knochenfische. Müller's Arch., 1850, p. 170.

branches, and, moreover, have stimulated the central end of the lateral branch. In the toad-fish, where the organs are normally exposed and not enclosed in canals, I have destroyed by thermo-cautery all of the organs upon one and upon both sides of the body. In general, it may be stated that the results indicate that the organs of the lateral line have a sensory function, closely connected with the motor organs and analogous to the functions of the ear, and hence may be regarded as organs of equilibrium.

Simple cutting of the lateral nerve on one side or even both sides, cutting of all the nerves supplying the lateral-line organs of both head and body, or destruction of all the organs themselves, does not seem to interfere much, if any, with the animal's equilibrium. I have observed at times an abnormally slow return to the normal position after an animal so operated upon has been turned upon his back, but whether this was due to dulling of a sense of equilibrium or to general weakness, I am unable to say. All these experiments were performed more than five years ago, however, and before experience had taught me to observe and interpret interferences with equilibrium, hence I would not now be willing to make a categorical statement regarding the effects of operations of this kind. The animals so operated upon are always much less active than before; they swim little, lie quiet, and rarely survive more than a day or two at most.

An extension of such operations has given more decided results. It occurred to me that a reduction of the motor mechanism employed in maintaining equilibrium might be an indirect aid in demonstrating a possible equilibrium function in the lateral-line organs. In the toad-fish, which spends much of its time lying upon the bottom of the sea, especially in holes under stones, the pectoral fins are enormously developed and seem to act as mechanical supports. Removal of these fins does not, however, of itself cause marked inconvenience in the maintenance of statical equilibrium or the performance of movements; the subsequent removal of the two smaller ventral fins is followed by no apparent genuine lack of the power to appreciate equilibrium and only a comparatively slight handicapping of the power of movement. It is remarkable how closely the actions of a fish deprived of these four fins resemble those of a normal fish; he is lively, vicious, quick in responding to mechanical stimuli, and certain in his movements; he guides himself accurately, turns about suddenly, and moves forward without lateral swaying of his body. But removal of the four fins combined with destruction of all the

organs of the lateral line (except the supraorbital ones, which are few in number and lie too deep for ready operation), produces a marked effect. This has been performed in several individuals. No genuine forced movements seem to follow, but there are decided evidences of a lack of the sense of equilibrium. This is manifested in various ways. There is decided uncertainty in movement, the animal swaying from side to side in forward progression. Such a fish is easily turned upon his side or back and lies quiet in this position. In one case, some two hours after the operation, the toad-fish was turned upon his back upon the bottom of his aquarium and remained thus for fifteen minutes, apparently without discomfort, and without attempting to return to the customary position. He was then returned to the latter by the hand. Such a fish swims irregularly upon his back or his side, with a general preference for the normal attitude. In one case in which the lateral organs of one side only were destroyed, and the pectoral and pelvic fins were removed, the power of maintaining equilibrium was found to be markedly weakened. When tested five hours after the operation, and presumably after the direct shock of it had passed away, the fish lay on his back when placed there; in swimming upward he thrust his head far out of water in much the same way as a fish deprived of his otolithic organs; and he showed the lateral swaying movements and uncertainty in forward progression, mentioned above. On the next day he exhibited the same phenomena. All the actions of a fish so operated upon remind one much of a lobster that has lost his otolithic sacs and chelæ.[1] The phenomena indicate strongly that the organs of the lateral line have something to do with equilibrium. In this connection it is of interest to know that Bonnier[2] has recently found that fishes whose lateral organs have been destroyed by galvano-cautery have largely lost the capacity of correct orientation in presence of disturbances in water.

It might be objected that the severity of the operation of cauterizing so many spots in the skin and removing the four fins might of itself be the cause of the disturbances of equilibrium above described. I have anticipated and nullified the possible force of such an objection by cauterizing an equal number of spots upon the skin of a nor-

[1] Bunting, M.: Ueber die Bedeutung der Otolithenorgane für die geotropischen Function von Astacus fluviatilis. Arch. f. d. ges. Physiol., 1893, liv, p. 531.

[2] Bonnier, P.: Sur le sens lateral. Comptes rendus de la soc. de biol., Paris, 1896, p. 917.

mal fish, carefully avoiding the lateral line, and then removing the four fins. Such an animal does not behave differently from one lacking the fins and not otherwise injured; he is active and certain in his movements, shows no lack of equilibrium, and in general closely resembles a normal fish.

But perhaps more significant than the above experiments on elimination is the result of stimulating the central end of the lateral nerve. In the dog-fish I have cut the nerve upon one side and stimulated it by an induced current just behind the head, thus including the nervous supply of all the organs of that side of the trunk. The result is perfectly coördinated, definite movements of the fins of both sides of the body. These fin-movements are the same as those called out by stimulating centrally the cut acoustic of the opposite side, and the same as those resulting from section of the acoustic of the same side. Thus, stimulating the left lateral nerve centrally caused: the two dorsal fins to move to the right; the caudal fin to move to the right; the left pectoral fin to move upward; the right pectoral fin to move downward; the two pelvic fins to move like the corresponding pectorals. This is exactly the result of stimulating the central stump of the right acoustic,[1] and also the exact result of cutting the left acoustic.[2] In the case of the acoustic I have shown that the result of stimulation is only what would be expected from a simultaneous and equal stimulation of the three ampullar branches of the acoustic. Since these branches are plainly equilibrative in function, it would seem to suggest strongly that the lateral nerve is also equilibrative. Occasionally, movements of the fins in directions opposite to those specified above take place, but they are by no means so constant or persistent, and, thus far, I have not attempted to determine the conditions of their appearance. In this connection it may be recalled that moderate or strong stimulation of the ampullæ of the semicircular canals causes movements of the eyes in a certain direction (principal function), and slight stimulation causes movements in exactly the opposite direction (subordinate function).[1] Movements of the trunk also result from stimulation of the lateral nerve, but thus far I have not endeavored to analyze them.

This is the extent of the experimenting that I have performed upon the lateral line, but, so far as it goes, it seems very suggestive. It would be interesting to test the lateral nerve at different parts of its course, and observe whether movements of the fins of different

[1] Lee: Journ. of physiol., 1894, xvii, p. 192. [2] *Ibid*, 1893, xv, p. 311.

segments result. Further, I have observed no eye-movements from lateral stimulation. It is conceivable that eye-movements may be mediated by the lateral-line organs of the head only, but so far I have not tested this possibility by stimulating the branches of the seventh nerve.

Without further work, which is already projected, it is impossible to specify in detail the nature of this possible equilibrative function of the sense-organs of the lateral line. The phenomena suggest Schulze's [1] idea of the possibility of appreciation of mass-movements of the water or of movements of the body through the water, just as the movements of the hairs of the cristæ through the inert endolymph mediate the appreciation of rotary movements of the body. Such a function seems more easily understood in the case of those fishes, such as the toad-fish, in which the sense-organs project freely to the outside, than in those in which the organs are enclosed within canals that open to the outside only at intervals. Yet in all species such a function seems to me *a priori* the most probable of all that have been suggested. The appreciation of rotary movements and that of progressive movements can hardly be separated here. It is not inconceivable nor improbable that, in addition to this function, contact with solid objects, such as the sand and stones at the bottom of the sea, may stimulate the organs and assist crudely in giving the fish a notion of his position in space. The structure of the organs suggests, as in the sense-organs of the ear, that they are pressure-organs of some kind. In this connection the work of Fuchs [2] is interesting. This investigator has shown by experiments upon Raja clavata and Raja asterias that touching the skin over the ventral canals of the head causes in most cases a negative variation of the current of rest in the cut nerves supplying these canals. He infers, not wholly with justification it seems to me, that the canals mediate the appreciation of changes of hydrostatic pressure.

In whatever specific way future experiments may prove the sense-organs in question to act, it is at least clear that those of the trunk are connected through the central nervous system with the muscles of the fins, and that a reflex arc is thus present, analogous in nature to that formed by the same motor mechanism with the acoustic nerve.

[1] Schulze, F. E.: Ueber die Sinnesorgane der Seitenlinie bei Fischen und Amphibien. Arch. f. mikr. Anat., 1870, vi, p. 62.

[2] Fuchs, S.: Ueber der unter der Haut liegenden Canalsysteme bei den Selachiern. Arch. f. d. ges. Physiol., 1895, lix, p. 454.

We must believe, moreover, that the impulses of whatever kind that come to the central nervous system from the organs in question assist in enabling the animal to maintain the equilibrium of his body: in other words, the organs of the lateral line are equilibrating organs.

Hence, a consideration of the physiology of the ear and the system of the lateral line, by showing that the two systems of organs are functionally analogous, would seem to offer indirect support to the morphological deduction that the former organ is a derivative of the latter. The primitive function, not improbably, was the appreciation of movements of the water against the body and movements of the body in the water, combined with appreciation of contact, and, hence, indirectly and crudely, of position in space; by the exercise of this function, through functional connection with the locomotor mechanism, the equilibrium of the body was maintained. In some unknown way a bit of this sensory system became cut off from the rest and enclosed within the skull; it still retained its power of appreciating bodily movements and contact, and this power became refined and differentiated; the capacity of appreciating rotary movements was separated from that dealing with progressive movements and position in space, and the two were associated with distinct organs, the semicircular canals on the one hand, and the otolithic organs on the other, which were appropriately constructed to subserve their respective functions. Thus a well-marked sensory organ for equilibrium was evolved in fishes. When aquatic animals began to leave the water and live for a shorter or longer time upon the land, and the possible advantage of a sense of hearing was presented, a portion of this sensory organ of movement became still farther differentiated; a new patch of sensory nerve-terminations appeared, the papilla acustica basilaris; apparatus for conveying the waves in the air directly to the membranous ear was developed; and thus the power of appreciating the movements that we call sound was acquired. By natural selection this was still more refined and specialized, the range of appreciation was extended, and the result is the mammalian cochlea with its great functional powers.

It seems to me that this explains naturally and in a manner not improbable the mysterious association in one organ of two functions at first sight so widely separated as equilibration and audition.

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